STIC Search Report
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STIC Database Tracking Number: 123775

TO:	From:
Richard Schnizer Location: REM-2C01/2C18 Art Unit: 1635 Wednesday, June 09, 2004 Case Serial Number: 09/555574	Noble Jarrell Location: Biotech-Chem Library Rem 1B71 Phone: 272-2556 Noble.jarrell@uspto.gov

Search Notes

Nothing here

123775

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: RICHARD SCHNIZER Examiner #: 76557 Date: 6/4/04
Art Unit: 1635 Phone Number ~~30~~ 2-0702 Serial Number: 09/555,574
Mail Box and Bldg/Room Location: REM 2C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

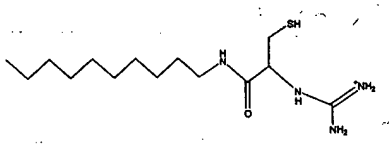
Title of Invention: TRANSFECTION PARTICLES

Inventors (please provide full names): Jean Paul Behr, Thomas Blessing, Ernst Wagner, Susanne Schueller

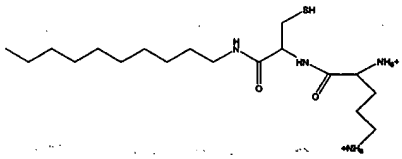
Earliest Priority Filing Date: 12/4/97

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the following structures:



and



I also need a search for attached claims 8-14, 16, 18, 21, and 49. Please give me a call to set up a time to discuss these claims.

Thanks
RS

****

STAFF USE ONLY

Searcher: Noble Jun	NA Sequence (#)	STN 552	
Searcher Phone #:	AA Sequence (#)	Dialog	
Searcher Location:	Structure (#) 2	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic	Dr.Link	
Date Completed: 6/4/04	Litigation	Lexis/Nexis	
Searcher Prep & Review Time: 60	Fulltext	Sequence Systems	
Clerical Prep Time:	Patent Family	WWW/Internet	
Online Time: 240	Other	Other (specify)	

Type of Search | **Vendors and cost where applicable**

PTO-1590 (8-01)

Amendments to the Claims

Claim 1 (currently amended): A transfection particle comprising one or more nucleic acid molecules condensed by organic cationic molecules, said particle being obtained by (1) condensing said one or more nucleic acid molecules with identical or different organic cationic precursor molecules without crosslinking any of said one or more nucleic acid molecules, and (2) thereafter obtaining cationic molecules by linking the precursor molecules to each other with one or more covalent bonds, wherein said one or more nucleic acid molecules remains condensed by said cationic molecules;

wherein the cationic precursor molecules comprise:

a) at least one functional group for binding to one or more other of said precursor molecules, wherein said functional group is a dimerizable or polymerizable functional group selected from the group consisting of thiols, acid hydrazides, aldehydes, amines, and ethylene residues that are suitably substituted to provide enamines upon reaction with an amine,

b) at least one lipophilic residue,

c) a non-toxic recipient backbone, and

d) a cationic group, ~~for binding to~~ <u>whereby said identical or different organic cationic precursor molecules complex said one or more</u> nucleic acid molecules.

Claim 2 (original): The transfection particle of claim 1, wherein the cationic molecules are lipids obtained by dimerization or oligomerization of cationic detergent precursor molecules.

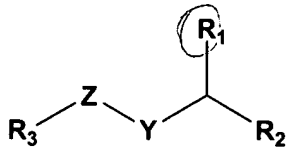
Claims 3-4 (canceled).

Claim 5 (previously presented): The transfection particle of claim 1, wherein the lipophilic residue is selected from the group consisting of lipophilic amides, esters and ethers.

Claim 6 (previously presented): The transfection particle of claim 1, wherein the functional group for binding to nucleic acid molecules is selected from an amine or derivative thereof.

Claim 7 (previously presented): The transfection particle of claim 6, wherein the functional group for binding to nucleic acid molecules is guanidine.

Claim 8 (previously presented): The transfection particle of claim 1, wherein the organic cationic precursor molecule is represented by general formula I



(I)

wherein

R_1 denotes (C_1-C_{10}-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, guanidyl, ornithylamino, or $-C(=X)-C_1-C_{10}$-alkylene, wherein the alkylene radical may

represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$ or a thiomonosaccharide;

R_3 denotes C_5-C_{30}-alkyl, straight chained or branched and optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_5-C_{30}-alkenyl, straight chained or branched having up to ten C=C-double bonds and is optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_5-C_{30}-alkynyl, straight chained or branched having up to ten C≡C-triple bonds and is optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_6-C_{10}-aryl optionally substituted, or

C_7-C_{16}-aralkyl optionally substituted, or a

C_5-C_{30}-alkyl-chain interrupted by up to 10 amino groups $-NR_4-$ and having optionally an amino-group which is optionally substituted by an amino acid;

R_4, R_5 and R_6 denote independently from each other hydrogen or C_1-C_4-alkyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or $-NR_4-$.

Claim 9 (previously presented): The transfection particle of claim 8, wherein the cationic precursor molecules correspond to general formula I, wherein

R_1 denotes (C_1-C_6-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, guanidyl, ornithylamino, or $-C(=X)-C_1-C_4$-alkylene, wherein the alkylene radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$ or a thiomonosaccharide;

R_3 denotes C_5-C_{20}-alkyl, straight chained or branched and optionally substituted with F, Cl, Br or $-NR_4R_5$, or

C_5-C_{20}-alkenyl, straight chained or branched having up to five C=C-double bonds and is optionally substituted with F, Cl, Br or $-NR_4R_5$, or

C_5-C_{20}-alkynyl, straight chained or branched having up to five C≡C-triple bonds and is optionally substituted with F, Cl, Br or $-NR_4R_5$, or

C_6-C_{10}-aryl optionally substituted with C_1-C_4-alkyl, F, Cl, Br or $-NR_4R_5$, or

C_7-C_{14}-aralkyl optionally substituted with C_1-C_4-alkyl, F, Cl, Br or $-NR_4R_5$, or

a C_5-C_{20}-alkyl chain interrupted by up to 10 amino groups $-NR_4-$ and having optionally an amino group which is optionally substituted by an amino acid;

R_4, R_5 and R_6 denote independently from each other hydrogen or C_1-C_4-alkyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or $-NR_4-$.

Claim 10 (previously presented): The transfection particle of claim 8, wherein the cationic precursor molecules correspond to general formula I, wherein

R_1 denotes (C_1-C_4-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, guanidyl, ornithylamino, or -C(=X)-C_1-C_4-alkyl, wherein the alkyl radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$, or a thiomonosaccharide;

R_3 C_5-C_{12}-alkyl, straight chained or branched and optionally substituted with F, Cl, Br or $-NH_2$, or a

C_5-C_{15}-alkyl chain interrupted by up to 7 amino groups $-NR_4-$ and having optionally an amino group which is optionally substituted by the amino acid cysteine;

R_4, R_5 and R_6 denote independently from each other hydrogen or methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl or tert-butyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or $-NR_4-$.

Claim 11 (previously presented): The transfection particle of claim 8, wherein the cationic precursor molecules correspond to the general formula I, wherein

R_1 denotes $-CH_2-SH$;

R_2 denotes $-NH_2$, $-NH_3^+$, $-C(=N^+H_2)NH_2$, guanidyl, ornithylamino, or -C(=O)-C_1-C_4-alkyl straight chained or branched and optionally substituted with F, Cl, Br or $-NH_2$,

or an ornithine radical or a S-galactosyl radical;

R_3 denotes a C_6-C_{15}-alkyl radical straight chained or branched and optionally substituted with F, Cl, Br or -NH_2;

Y denotes C=O;

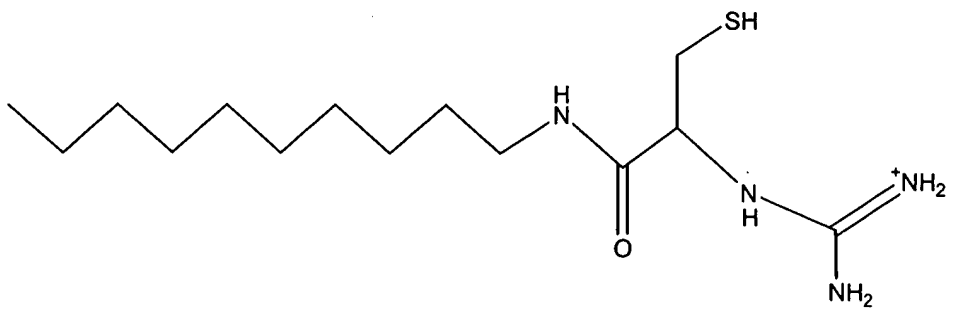
Z denotes O or -NH-.

Claim 12 (previously presented): The transfection particle of one of claims 8 to 11, wherein R_2 is guanidine or ornithylamino.

Claim 13 (previously presented): The transfection particle of claims 8 to 11, wherein R_3 is a decyl radical.

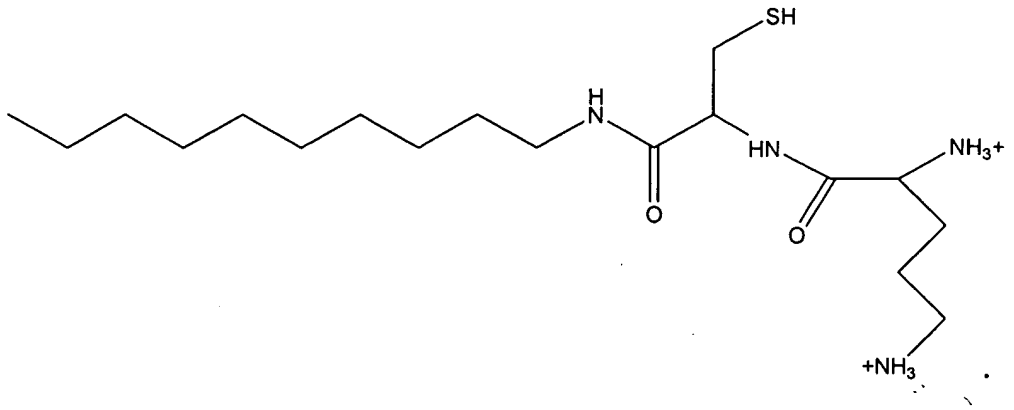
Claim 14 (previously presented): The transfection particle of one of claims 8 to 11, wherein R_1 is a methylenethiol, R_2 is guanidine, R_3 is a straight chained decyl radical, Y is a carbonyl, Z is an amine, and pharmaceutically acceptable salts thereof.

Claim 15 (previously presented): The transfection particle of claim 14, wherein the cationic molecule has the following formula:



Claim 16 (previously presented): The transfection particle of one of claim 8 to 11, wherein R_1 is a methylenethiol, R_2 is an ornithylamino, R_3 is a decane, Y is a carbonyl, Z is an amine, and pharmaceutically acceptable salts thereof.

Claim 17 (previously presented): The transfection particle of claim 16, wherein the cationic molecule has the following structure:



Claim 18 (previously presented): The transfection particle of one of claim 8 to 10, wherein the monosaccharide which is bonded via a sulfur atom is selected from the group consisting of galactose, lactose, glucose, arabinose, fructose, sorbose, xylose, ribose, mannose each of them in their D- or L-form.

Claim 19 (original): The transfection particle of claim 1, wherein the cationic precursor molecule is a polyamine.

Claim 20 (original): The transfection particle of claim 19, wherein the cationic precursor molecule is a spermine derivative.

Claim 21 (original): The transfection particle of claim 20, wherein the cationic precursor molecule is spermine-N1,N12-bis-cysteineamide.

Claim 22 (previously presented): The transfection particle of claim 1, wherein the one or more covalent bonds between the cationic molecules are degradable under reductive or slightly acidic conditions, or in the presence of enzymes.

Claim 23 (original): The transfection particle of claim 1 which comprises a single nucleic acid molecule.

Claim 24 (original): The transfection particle of claim 1 or 23, wherein the nucleic acid molecule is a DNA molecule.

Claim 25 (original): The transfection particle of claim 24, wherein the DNA molecule is a plasmid.

Claim 26 (original): The transfection particle of claim 1, wherein the nucleic acid molecule is an RNA molecule.

Claim 27 (previously presented): The transfection particle of claim 1, characterized in that it is linked via one or more covalent bonds to one or more members of the group consisting of protein ligands, sugar residues, fusogenic peptides, viruses, adenoviruses, and combinations thereof.

Claim 28 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group are linked via said one or more covalent bonds to the cationic molecules.

Claim 29 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group are linked via said one or more covalent bonds to nucleic acid binding molecules that are present in addition to the cationic molecules.

Claim 30 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group is a protein ligand.

Claim 31 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group is a sugar residue.

Claim 32 (previously presented): The transfection particle of claim 31, wherein the sugar residue is galactose.

Claim 33 (previously presented): The transfection particle of claim 31, wherein the sugar residue is mannose.

Claims 34-36 (canceled).

Claim 37 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group is a fusogenic peptide.

Claim 38 (previously presented): The transfection particle of claim 27, wherein said one or more members of the group is a virus.

Claim 39 (original): The transfection particle of claim 38, wherein the virus is an adenovirus.

Claim 40 (previously presented): A method for preparing transfection particles of claim 1, wherein cationic precursor molecules are added to nucleic acid molecules in a suitable buffer, allowed to form complexes with the nucleic acid and allowed to covalently link to identical or different cationic precursor molecules on the nucleic acid template.

Claim 41 (original): The method of claim 40, wherein the cationic precursor molecules are lipophilic and are allowed to covalently link under mild oxidative conditions.

Claims 42-44 (canceled).

Claim 45 (previously presented): A kit of parts comprising one or more nucleic acid molecules, one or more cationic precursor molecules, suitable buffers, and other reagents or mechanical devices that are useful for preparation or purification of a transfection particle of claim 1.

Claim 46 (previously presented): The kit of parts of claim 45 comprising in addition one or more members of the group consisting of nucleic acid binding molecules that are present in addition to the cationic molecules, protein ligands, sugar residues, fusogenic peptides, viruses, adenoviruses, and combinations thereof.

Claim 47 (canceled).

Claim 48 (previously presented): A transfection particle comprising:

a) one or more nucleic acid molecules;

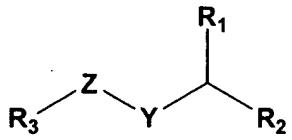
b) identical or different organic cationic precursor molecules linked to each other via one or more covalent bonds;

wherein said precursor molecules are ionically associated with said one or more nucleic acid molecules without forming any crosslinks between said nucleic acid molecules and said cationic precursor molecules, thereby condensing said one or more nucleic acid molecules.

Claim 49 (previously presented): A transfection particle comprising one or more nucleic acid molecules condensed by organic cationic molecules, said particle being obtained by (1) condensing said one or more nucleic acid molecules with identical or

different organic cationic precursor molecules without crosslinking any of said one or more nucleic acid molecules, and (2) thereafter obtaining cationic molecules by linking the precursor molecules to each other with one or more covalent bonds, wherein said one or more nucleic acid molecules remains condensed by said cationic molecules;

wherein the organic cationic precursor molecule is represented by general formula I



(I)

wherein

R_1 denotes (C_1-C_{10}-alkylene)-SH, wherein the alkylene radical may represent a straight chained or branched hydrocarbon;

R_2 denotes $-NR_4R_5$, $-NHR_4R_5^+$, $-N(R_4)_2R_5^+$, $-C(=NR_4)NR_5R_6$, guanidyl, ornithylamino, or -C(=X)-C_1-C_{10}-alkylene, wherein the alkylene radical may represent a straight chained or branched hydrocarbon and may be substituted by up to four amino radicals $-NR_4R_5$ or a thiomonosaccharide;

R_3 denotes C_5-C_{30}-alkyl, straight chained or branched and optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_5-C_{30}-alkenyl, straight chained or branched having up to ten C=C-double bonds and is optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_5-C_{30}-alkynyl, straight chained or branched having up to ten C≡C-triple bonds and is optionally substituted with one or more halogen atoms or dialkyl amino groups, or

C_6-C_{10}-aryl optionally substituted, or

C_7-C_{16}-aralkyl optionally substituted, or a

C_5-C_{30}-alkyl-chain interrupted by up to 10 amino groups -NR_4- and having optionally an amino-group which is optionally substituted by an amino acid;

R_4, R_5 and R_6 denote independently from each other hydrogen or C_1-C_4-alkyl;

X denotes O or S;

Y denotes C=O or C=S and

Z denotes O, S or -NR_4-.

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L3   (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  C18H38N4O2S/MF
L4   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND CYSTEINAMIDE
L5             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L4
L6               STR
L7               SCR 2021
L8               SCR 2039 OR 2050 OR 2049 OR 2053 OR 2043 OR 2054
L9               SCR 1771
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L11              STR
L12         1065 SEA FILE=REGISTRY SUB=L10 CSS FUL L11

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L16  (       461)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("WAGNER ERNST"/AU OR "WAGNER
L17  (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SCHUELLER S"/AU
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L19  (      3289)SEA FILE=HCAPLUS ABB=ON  PLU=ON  BOEHRINGER INGELHEIM?/CS,PA
L20           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR L
L21            4 L5
L22            4 L21 AND L14-17
                 S L21 AND L8-19
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L24         1191 L13 (L) RACT+NT/RL
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L26            7 L24 AND L18-19
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L29       657989 NUCLEIC ACIDS+OLD,NT/CT
L30         5241 NUCLEIC ACID LIBRARY+NT/CT
L31         9067 COMBINATORIAL LIBRARY+NT/CT
L32           65 CHEMICAL LIBRARY/CT
L33        84991 NUCLEOSIDES+OLD,NT/CT
L34       288337 NUCLEOTIDES+NT/CT
L35           33 L28 AND L29-34

     FILE 'REGISTRY' ENTERED AT 15:00:47 ON 09 JUN 2004

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L36              TRA L20 1- RN :       45 TERMS

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L37           45 SEA L36
L38            5 L12 AND L37
L39            8 L37 AND S/ELS
L40            4 L39 AND (C28 H60 N6 O2 S OR C24 H50 N4 O2 S OR C22 H46 N4 O2 S
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L43            1 C22H46N4O2S
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L45            1 C28H60N6O2S
                 SEL RN L40
L46            0 E1-4/CRN
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L47 8 L40
L48 8 L47 AND L14-17
L49 7 L47 AND L18-19
L50 2 L35 AND (PHOTOCHEMICAL REDUCTION OR DEHALOGENATION)/TI

FILE 'REGISTRY' ENTERED AT 17:01:38 ON 09 JUN 2004
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L54 8 L53
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L56 7 L54 AND L18-19

=> b hcap
FILE 'HCAPLUS' ENTERED AT 17:12:41 ON 09 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 9 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 8 Jun 2004 (20040608/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L20 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:941166 HCAPLUS
DN 140:140109
ED Entered STN: 03 Dec 2003
TI Tumor-targeted gene transfer with DNA polyplexes
AU Ogris, Manfred; **Wagner, Ernst**
CS Pharmaceutical Biotechnology, Center for Pharmaceutical Research,
Ludwig-Maximilians-University, Munich, D-81377, Germany
SO Biotechnology Intelligence Unit (2003), 7(Synthetic DNA Delivery Systems),
81-91
CODEN: BIUNF9; ISSN: 1527-246X
PB Landes Bioscience
DT Journal; General Review
LA English
CC 3-0 (Biochemical Genetics)
Section cross-reference(s): 1, 13
AB A review. Systemic gene delivery systems are needed for therapeutic

applications; in some situations, target cells might be spread throughout the organism, as in the case of cancer metastases, which can be reached only via the systemic route. Within the class of nonviral vectors, polymer-based **transfection particles** named DNA polyplexes and lipid-based systems named DNA lipoplexes are being developed for this purpose. For systemic circulation, masking the surface charge of DNA complexes has to be accomplished to avoid interactions with plasma components, erythrocytes, and the reticuloendothelial system. Among other vector formulations, polyplexes based on polyethylenimine (PEI), shielded with polyethylene glycol (PEG), and linked to the receptor binding ligands transferrin (Tf) or epidermal growth factor (EGF) have been developed. Complexes were found to mediate efficient gene transfer into tumor cell lines in a receptor-dependent and cell-cycle-dependent manner. Systemic administration of surface-shielded Tf-PEI polyplexes into the tail vein of mice resulted in preferential gene delivery into distantly growing s.c. tumors. In contrast, application of pos. charged PEI polyplexes directed gene transfer primarily to the lung.

ST review tumor targeting gene transfer DNA polyplex

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA complexes; tumor-targeted gene transfer with DNA polyplexes)

IT DNA
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes, polyplex; tumor-targeted gene transfer with DNA polyplexes)

IT Transferrins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyethylenimine conjugates; tumor-targeted gene transfer with DNA polyplexes)

IT Gene therapy
Mouse
Neoplasm
(tumor-targeted gene transfer with DNA polyplexes)

IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-targeted gene transfer with DNA polyplexes)

IT 9002-98-6, Polyethylenimine 9002-98-6D, Polyethylenimine, transferrin factor conjugates 25322-68-3, Polyethylene glycol
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-targeted gene transfer with DNA polyplexes)

RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(14) Dong, Y; Nucleic Acids Res 1993, V21, P771 HCAPLUS

(15) Emi, N; Biochem Biophys Res Commun 1997, V231, P421 HCAPLUS
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(18) Finsinger, D; Gene Ther 2000, V7, P1183 HCAPLUS
(19) Gautam, A; Gen Ther 2002, V9, P353 HCAPLUS
(20) Goula, D; Gene Ther 1998, V5, P1291 HCAPLUS
(21) Goula, D; Gene Ther 2000, V7, P499 HCAPLUS
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L20 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:234067 HCAPLUS
DN 139:128510
ED Entered STN: 26 Mar 2003

TI Tumor-Targeted Gene Transfer with DNA Polyplexes
AU Ogris, Manfred; **Wagner, Ernst**
CS Center of Drug Research, Pharmaceutical Biology-Biotechnology, Ludwig-Maximilians-University Munich, Munich, D-81377, Germany
SO Somatic Cell and Molecular Genetics (2002), 27(1-6), 85-95
CODEN: SCMGDN; ISSN: 0740-7750
PB Kluwer Academic/Plenum Publishers
DT Journal; General Review
LA English
CC 3-0 (Biochemical Genetics)
Section cross-reference(s): 14
AB A review. Systemic gene delivery systems are needed for therapeutic applications; in some situations, target cells might be spread throughout the organism, as in the case of cancer metastases, which can be reached only via the systemic route. Within the class of nonviral vectors, polymer-based **transfection particles** named DNA polyplexes and lipid-based systems named DNA lipoplexes are being developed for this purpose. For systemic circulation, masking the surface charge of DNA complexes has to be accomplished to avoid interactions with plasma components, erythrocytes, and the reticuloendothelial system. Among other vector formulations, polyplexes based on polyethylenimine (PEI), shielded with polyethylene glycol (PEG), and linked to the receptor binding ligands transferrin (Tf) or epidermal growth factor (EGF) have been developed. Complexes were found to mediate efficient gene transfer into tumor cell lines in a receptor-dependent and cell-cycle-dependent manner. Systemic administration of surface-shielded Tf-PEI polyplexes into the tail vein of mice resulted in preferential gene delivery into distantly growing s.c. tumors. In contrast, application of pos. charged PEI polyplexes directed gene transfer primarily to the lung.
ST review cancer therapy gene transfer polyethylenimine polyplex
IT DNA
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes, polyplexes and lipoplexes; polyplexes based on polyethylenimine, shielded with polyethylene glycol, and linked to the receptor binding ligands transferrin or epidermal growth factor have been developed for gene therapy)
IT Genetic vectors
(polyplexes and lipoplexes; polyplexes based on polyethylenimine, shielded with polyethylene glycol, and linked to the receptor binding ligands transferrin or epidermal growth factor have been developed for gene therapy)
IT Polyoxyalkylenes, biological studies
Transferrins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyplexes based on polyethylenimine, shielded with polyethylene glycol, and linked to the receptor binding ligands transferrin or epidermal growth factor have been developed for gene therapy)
IT Antitumor agents
Drug delivery systems
Gene therapy
Transformation, genetic
(tumor-targeted gene transfer with DNA polyplexes)
IT 25322-68-3, Polyethylene glycol 62229-50-9, Epidermal growth factor
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyplexes based on polyethylenimine, shielded with polyethylene glycol, and linked to the receptor binding ligands transferrin or epidermal growth factor have been developed for gene therapy)

IT 9002-98-6, Polyethylenimine
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyplexes based on; tumor-targeted gene transfer with DNA polyplexes)
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(47) Plank, C; Hum Gene Ther 1996, V7, P1437 HCAPLUS
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(49) Sokoloff, A; Mol Ther 2000, V2, P131 HCAPLUS
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L20 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:350540 HCAPLUS
DN 138:112277
ED Entered STN: 10 May 2002
TI Dimerizable cationic detergents condense plasmid DNA into 30 nm **particles** and **transfect** cells in vitro
AU Dauty, E.; Remy, J. S.; **Blessing, T.**; **Behr, J. P.**
CS Faculte de Pharmacie de Strasbourg, Laboratoire de Chimie Genetique associe CNRS/**Universite Louis Pasteur**, Illkirch, 67401, Fr.
SO Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1135-1136
Publisher: Controlled Release Society, Minneapolis, Minn.
CODEN: 69CNY8
DT Conference
LA English
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
AB In the present investigation, we reported the biophys. and biol. properties of the ornithinylcysteinyltetradecylamide (C14COrn). This new dimerizable detergent condenses plasmid DNA into monomol. particles of 30 nm. This complexes are mobile in agarose gel and exhibit a typical lipid/DNA supramol. structure. When the complexes are large and cationic they show a transfection efficiency comparable to that obtained with the most potent vectors.
ST dimer cationic detergent plasmid DNA transfection
IT Detergents
(cationic; dimerizable cationic detergents condense plasmid DNA into 30-nm **particles** and **transfect** cells)
IT DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; dimerizable cationic detergents condense plasmid DNA into 30-nm **particles** and **transfect** cells)
IT Drug delivery systems
Gene therapy
Transformation, genetic
(dimerizable cationic detergents condense plasmid DNA into 30-nm **particles** and **transfect** cells)
IT DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dimerizable cationic detergents condense plasmid DNA into 30-nm **particles** and **transfect** cells)
IT 227176-25-2D, DNA complexes

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detergent; dimerizable cationic detergents condense plasmid DNA into 30-nm **particles** and **transfect** cells)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L20 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:758911 HCAPLUS
DN 137:68001
ED Entered STN: 18 Oct 2001

TI DNA/polyethylenimine **transfection particles**: Influence of ligands, polymer size, and PEGylation on internalization and gene expression

AU Ogris, Manfred; Steinlein, Peter; Carotta, Sebastian; Brunner, Sylvia; **Wagner, Ernst**
CS Institute of Biochemistry, University of Vienna, Vienna, Austria

SO PharmSci [online computer file] (2001), 3(3), No pp. given
CODEN: PHARFY; ISSN: 1522-1059
URL: http://www.pharmsci.org/scientificjournals/pharmsci/journal/01_21.htm1
PB American Association of Pharmaceutical Scientists
DT Journal; (online computer file)
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 3

AB Receptor-binding ligands have been incorporated into DNA/polyethylenimine (PEI) complexes to enhance cell binding and cellular internalization. This study characterizes receptor-mediated uptake of DNA/PEI complexes on a cellular basis. A novel assay based on flow cytometry was applied, discriminating between total cell-associated and extracellularly bound DNA complexes. Receptor-mediated uptake of ligand-containing DNA/PEI (mol. weight, 800 kd) complexes was found to occur quickly (within 1 h), whereas unspecific uptake through adsorptive endocytosis is less efficient or requires extended periods to reach the same degree of internalization. Rapid, receptor-mediated internalization requires a small complex size; however, large, aggregated complexes show higher gene expression. Using PEI 25 kd conjugated to large proteins such as transferrin or antibodies, improper condensation with DNA leads to suboptimal uptake and gene expression, whereas partial replacement of ligand-PEI with unconjugated PEI increases both uptake and transfection. In contrast, the 8 kd protein epidermal growth factor conjugated to PEI 25 kd properly condenses DNA and mediates specific uptake into human adenocarcinoma (KB) cells. Modification of the complex surface with appropriate amts. of poly(ethylene glycol) (PEG) does not block ligand-mediated internalization. A higher degree of PEGylation reduces the internalization of transferrin or antibody-containing complexes to a level similar to that of ligand-free complexes. In contrast, epidermal growth factor-mediated uptake is less affected by excessive PEGylation.

ST PEGylation DNA polyethylenimine transfection gene delivery expression

IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; influence of ligands, polymer size, and PEGylation on

internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression; influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT Genetic vectors
Genetic vectors
Transformation, genetic
(influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT Transferrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT 62229-50-9, Egf
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

IT 9002-98-6D, Polyethylenimine, complexes 25322-68-3D, Polyethyleneglycol, conjugates 26913-06-4D, Polyethylenimine, complexes
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of ligands, polymer size, and PEGylation on internalization of DNA/polyethylenimine **transfection particles** and gene expression)

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L20 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:636468 HCAPLUS
DN 135:252520
ED Entered STN: 02 Sep 2001
TI Dimerizable Cationic Detergents with a Low cmc Condense Plasmid DNA into Nanometric **Particles** and **Transfect** Cells in Culture
AU Dauty, Emmanuel; Remy, Jean-Serge; **Blessing, Thomas**; **Behr, Jean-Paul**
CS Laboratoire de Chimie Genetique, CNRS/**Universite Louis Pasteur** de Strasbourg Faculte de Pharmacie, Illkirch, 67401, Fr.
SO Journal of the American Chemical Society (2001), 123(38), 9227-9234
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 9, 26, 63
AB The size of condensed DNA particles is a key determinant for in vivo diffusion and gene delivery to cells. Gene mols. can be individually compacted by cationic thiol detergents into nanometric particles that are stabilized by oxidative conversion of the detergent into a gemini lipid. To reach the other goal, gene delivery, a series of cationic thiol detergents with various chain lengths (C12-C16) and headgroups (ornithine or spermine) was prepared, using a versatile polymer-supported synthetic strategy. Critical micelle concns. and thiol oxidation rates of the detergents were measured. The formation and stability of complexes formed with plasmid DNA, as well as the size, ξ-potential, morphol., and transfection efficiency of the particles were investigated. Using the tetradecane/ornithine detergent, a solution of 5.5 Kpb plasmid DNA mols. was converted into a homogeneous population of 35 nm particles. The same detergent, once oxidized, exhibited a typical lipid phase internal structure and was capable of effective cell transfection. The particle size did not increase with time. Surprisingly, the gel electrophoretic mobility of the DNA complexes was found to be higher than that of plasmid DNA itself. Favorable in vivo diffusion and intracellular trafficking properties may thus be expected for these complexes.
ST **transfection** nanometric **particle** plasmid DNA tetradecane ornithine detergent; detergent cationic thiol cmc oxidn plasmid DNA complex transfection
IT Molecular association
((C14COrn)/DNA complexes; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(closed circular; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT Critical micelle concentration
Nanoparticles
Particle shape
Solid phase synthesis
Transformation, genetic
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT Particle size
(nanoscale; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT Plasmids
(pCMV-luc; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT Bond formation
(sulfur-sulfur; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT 173966-44-4DP, bead-grafted 361525-73-7P
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT 70-26-8, Ornithine 124-22-1, Dodecylamine 143-27-1, Hexadecylamine 2016-42-4, Tetradecylamine 142601-71-6 186002-24-4 362046-48-8D, NovaSyn MMT alcohol resin, PEG derivative
RL: RCT (Reactant); RACT (Reactant or reagent)
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT 227176-25-2P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

IT 227176-24-1P 361525-74-8P 361525-75-9P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric **particles** and **transfect** cells in culture)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L20 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:441642 HCAPLUS
DN 131:180305
ED Entered STN: 20 Jul 1999
TI Mannose polyethylenimine conjugates for targeted DNA delivery into dendritic cells
AU Diebold, Sandra S.; Kursa, Margaretha; **Wagner, Ernst**; Cotten, Matt; Zenke, Martin
CS Max-Delbriick-Center for Molecular Medicine, Berlin, D-13092, Germany
SO Journal of Biological Chemistry (1999), 274(27), 19087-19094
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 15
AB Cell surface-bound receptors represent suitable entry sites for gene delivery into cells by receptor-mediated endocytosis. Here we have taken advantage of the mannose receptor that is highly expressed on antigen-presenting dendritic cells for targeted gene transfer by employing mannosylpolyethylenimine (ManPEI) conjugates. Several ManPEI conjugates were synthesized and used for formation of ManPEI/DNA transfection complexes. Conjugates differed in the linker between mannose and polyethylenimine (PEI) and in the size of the PEI moiety. We demonstrate that ManPEI transfection is effective in delivering DNA into mannose receptor-expressing cells. Uptake of ManPEI/DNA complexes is receptor-specific, since DNA delivery can be competed with mannosylated albumin. Addnl., incorporation of adenovirus **particles** into **transfection** complexes effectively enhances transgene expression. This is particularly important for primary immunocompetent dendritic cells. It is demonstrated here that dendritic cells transfected with ManPEI/DNA complexes containing adenovirus particles are effective in activating T cells of T cell receptor transgenic mice in an

antigen-specific fashion.
ST mannose PEI conjugate DNA complex transformation dendritic cell
IT Human adenovirus
(DNA complexes containing particles of; mannose polyethylenimine conjugates for targeted DNA delivery into dendritic cells)
IT Dendritic cell
Transformation, genetic
(mannose polyethylenimine conjugates for targeted DNA delivery into dendritic cells)
IT Mannose receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mannose polyethylenimine conjugates for targeted DNA delivery into dendritic cells)
IT 3458-28-4DP, Mannose, conjugates with PEI 9002-98-6DP, PEI, conjugates with mannose
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(mannose polyethylenimine conjugates for targeted DNA delivery into dendritic cells)
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L20 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:395896 HCAPLUS
DN 129:140540
ED Entered STN: 29 Jun 1998
TI Influence of the DNA complexation medium on the transfection efficiency of lipospermine/DNA particles
AU Kichler, A.; Zauner, W.; Ogris, M.; **Wagner, E.**
CS Institute of Biochemistry, University of Vienna, Austria
SO Gene Therapy (1998), 5(6), 855-860
CODEN: GETHEC; ISSN: 0969-7128
PB Stockton Press
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB Dioctadecylamidoglycylspermine (DOGS, Transfectam) is a cationic lipid able to interact with DNA to form complexes that mediate efficient gene transfer into various eukaryotic cells. The state of condensation of the plasmid changes with the medium composition We therefore investigated to what extent the DNA condensation buffer influences the transfection efficiency of **Transfectam**/DNA **particles.** Our results show that in a variety of cell lines, a greater than 100-fold difference in luciferase gene expression is observed with Transfectam/DNA complexes at a +/- charge ratio of 0.75 depending on the conditions of complex formation. The best transfection conditions consisted of particles formed in RPMI medium, NaHCO3/Na2HPO4 or sodium citrate solns. Mixing in a 150 mM sodium chloride solution (as recommended) resulted in lower gene expression. When the helper lipid 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) was present in the DNA/cationic lipid formulation, the increase in reporter activity was also observed, although to a lower extent. Thus, choosing the optimal conditions for formulating DNA/lipid complexes considerably reduces the amount of lipid and DNA needed to obtain maximum gene transfer.
ST DNA lipid complex optimization gene therapy
IT Buffers
Drug delivery systems
Gene therapy
Transformation, genetic
(influence of DNA complexation medium on transfection efficiency of lipospermine/DNA particles)
IT DNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(influence of DNA complexation medium on transfection efficiency of lipospermine/DNA particles)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transfer; influence of DNA complexation medium on transfection efficiency of lipospermine/DNA particles)
IT 9014-00-0, Luciferase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of DNA complexation medium on transfection efficiency of lipospermine/DNA particles)
IT 144-55-8, Sodium carbonate (NaHCO3), biological studies 994-36-5, Sodium citrate 4004-05-1, DOPE 7558-79-4, Sodium phosphate (Na2HPO4) 7647-14-5, Sodium chloride, biological studies 124050-77-7, Transfectam
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of DNA complexation medium on transfection efficiency of lipospermine/DNA particles)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L20 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:505720 HCAPLUS
DN 122:306487
ED Entered STN: 22 Apr 1995
TI Efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids
AU Kichler, Antoine; Remy, Jean-Serge; Boussif, Otmane; Frisch, Benoit; Boeckler, Christophe; **Behr, Jean-Paul**; Schuber, Francis
CS Lab. Chimie Bioorg., Fac. Pharmacie, Strasbourg-Illkirch, 67400, Fr.
SO Biochemical and Biophysical Research Communications (1995), 209(2), 444-50
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
CC 1-12 (Pharmacology)

Section cross-reference(s): 63
AB The presence of thiol-reactive phospholipid derivs., such as N-(4-(p-maleimidophenyl)butyryl)dipalmitoylphosphatidylethanolamine (MPB-DPPE), in elec. neutral lipospermine/DNA particles results in more than a 100-fold increased transfection efficiency of human hepatoma HepG2 cells and murine 3T3 fibroblasts. These effects could be ascribed to the presence of thiol-reactive functions, such as maleimide, bromoacetamide and dithiopyridyl linkage, on the **transfecting particles** . The authors propose that such particles react with thiol groups present at the surface of the cells, leading to their covalent anchoring, a process that is probably followed by an endocytosis of the complex.
ST gene delivery lipospermine thiol reactive phospholipid
IT Transformation, genetic
(efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)
IT Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiol-reactive; efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)
IT Therapeutics
(geno-, efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)
IT 113846-31-4 126165-91-1 163277-91-6 163277-92-7 163277-93-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)
IT 71-44-3, Spermine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipo-; efficient gene delivery with neutral complexes of lipospermine and thiol-reactive phospholipids)

L20 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:647368 HCAPLUS
DN 121:247368
ED Entered STN: 26 Nov 1994
TI Gene Transfer with a Series of Lipophilic DNA-Binding Molecules
AU Remy, Jean-Serge; Sirlin, Claude; Vierling, Pierre; **Behr, Jean-Paul**
CS Laboratoire de Chimie genetique, Faculte de Pharmacie de Strasbourg, Illkirch, F-67401, Fr.
SO Bioconjugate Chemistry (1994), 5(6), 647-54
CODEN: BCCHES; ISSN: 1043-1802
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
AB Synthetic gene transfer vectors could be an attractive alternative to biol. vehicles for gene therapy. In an effort to improve the previously developed lipopolyamine-mediated transfection technique, various amphiphilic DNA-binding mols. have been synthesized. Besides Transfectam, several lipospermines display very high gene delivery levels. The structure-activity relation obtained points to the central role played by the polyamine headgroup in condensing the plasmid and binding it to the cell surface, provided the hydrophobic moiety is capable to generate nonmicellar mesomorphic structures. It also highlights other favorable (albeit more speculative) properties shared by protonable lipospermines as

compared to quaternary ammonium-bearing lipids, such as their ability to act as a buffer and their strong affinity for chromatin. The former property may prevent the pH decrease along the degradative lysosomial pathway. The ability to bind to chromatin even in the presence of endogeneous polyamines should have two consequences: a nuclear tropism of the **transfecting particles** and plasmid uncoating in the nucleus by competitive dilution of the lipopolyamine into an ocean of DNA.

ST gene transfer lipospermine transfectam

IT Transformation, genetic
(gene transfer with series of lipophilic DNA-binding mols.)

IT Gene
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene transfer with series of lipophilic DNA-binding mols.)

IT Genetic vectors
(preparation of and gene transfer with series of lipophilic DNA-binding mols.)

IT 71-44-3P, Spermine
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(lipo-; preparation of and gene transfer with series of lipophilic DNA-binding mols.)

IT 122342-03-4P 158730-40-6P 158730-41-7P 158730-42-8P 158730-43-9P
158730-44-0P 158730-45-1P 158730-46-2P 158730-47-3P 158730-48-4P
158730-49-5P 158730-50-8P 158730-51-9P 158730-52-0P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation of and gene transfer with series of lipophilic DNA-binding mols.)

L20 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:474680 HCAPLUS
DN 121:74680
ED Entered STN: 20 Aug 1994
TI Synthetic gene transfer vectors
AU **Behr, Jean Paul**
CS Lab. Chim. Genet., Fac. Pharm., Strasbourg, F-67401, Fr.
SO Pure and Applied Chemistry (1994), 66(4), 827-35
CODEN: PACHAS; ISSN: 0033-4545
DT Journal; General Review
LA English
CC 3-0 (Biochemical Genetics)
AB A review with 25 refs. Gene transfer into mammalian cells is a prerequisite to gene therapy. Designed synthetic DNA carriers could be attractive alternatives to presently used viral vectors. Toward this end, lipopolyamines have been developed, which spontaneously condense DNA and coat it with a cationic lipid layer. The resulting nucleolipidic **particles transfect** efficiently various eukaryotic cells.

ST review gene transfer vector lipopolyamine

IT Transformation, genetic
(of genes into mammalian cells, synthetic vectors and lipopolyamines for)

IT Gene, animal
RL: PRP (Properties)
(transfer of, into mammalian cells, synthetic vectors and lipopolyamines for)

L20 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:574974 HCAPLUS
DN 119:174974
ED Entered STN: 30 Oct 1993
TI Gene transfer optimization with lipospermine-coated DNA
AU Barthel, Fabrice; Remy, Jean Serge; Loeffler, Jean Philippe; **Behr, Jean Paul**
CS Inst. Physiol., CNRS, Strasbourg, F-67000, Fr.
SO DNA and Cell Biology (1993), 12(6), 553-60
CODEN: DCEBE8; ISSN: 1044-5498
DT Journal
LA English
CC 3-2 (Biochemical Genetics)
AB Designed synthetic DNA carriers represent an attractive alternative to the widely used calcium phosphate gene transfer technique. In this context, the authors developed a class of nucleic acid binding lipids, the lipopolyamines, which spontaneously condense DNA on a cationic lipid layer. The resulting nucleolipidic **particles transfect** most animal cells efficiently. However, compaction depends on many exptl. factors, some of which have been varied here to give optimal transfection efficiency. When plasmid condensation by the lipospermine is performed in the absence of competing polyions or serum proteins, or when the gene of interest is diluted into carrier DNA, transfection efficiency is increased by 2-3 orders of magnitude. With these improvements, chloramphenicol acetyl transferase activity resulting from transfection of as little as 25 ng could easily be detected by a nonradioactive ELISA test.
ST genetic transformation lipospermine coated DNA
IT Transformation, genetic
(of animal cells, using lipospermine-coated DNA, optimization of)
IT Amines, uses
RL: USES (Uses)
(poly-, fatty, DNA coated with, for genetic transformation of animal cells)

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FILE 'HOME' ENTERED AT 17:12:54 ON 09 JUN 2004

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DICTIONARY FILE UPDATES:   8 JUN 2004  HIGHEST RN 690955-30-7

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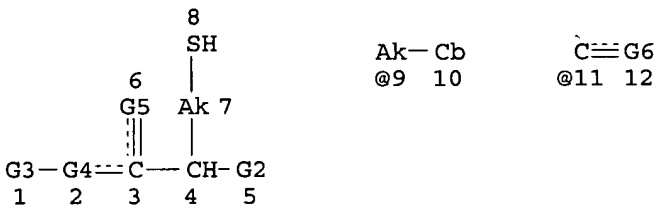


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  12

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L9                SCR 1771
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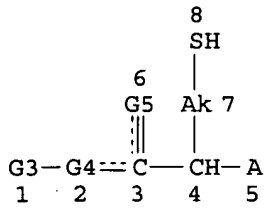

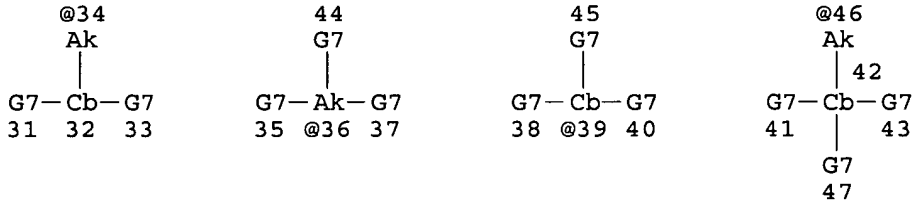

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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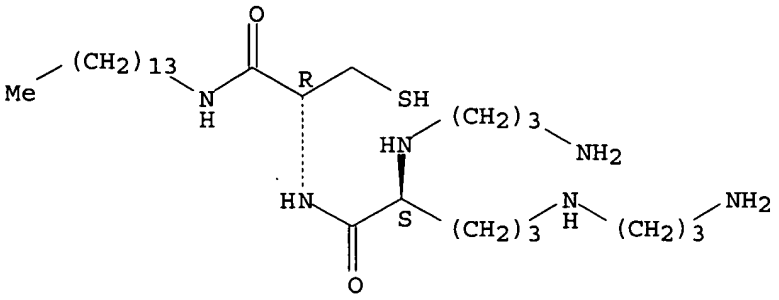
L40 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN Date??
RN **361525-75-9** REGISTRY
CN L-Cysteinamide, N2,N5-bis(3-aminopropyl)-L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C28 H60 N6 O2 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.



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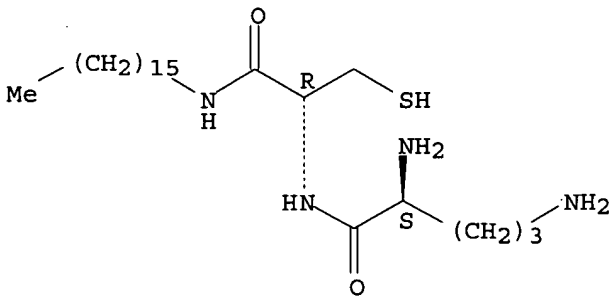
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L40 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **361525-74-8** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-hexadecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H50 N4 O2 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.



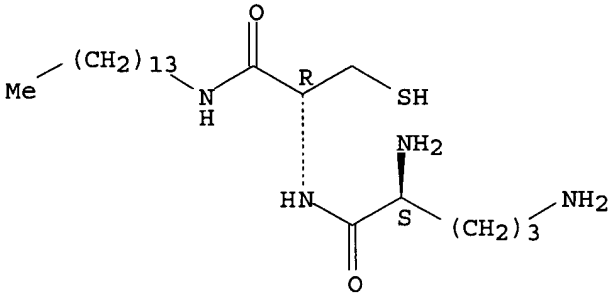
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L40 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **227176-25-2** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C22 H46 N4 O2 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Conference; Journal; Patent

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.

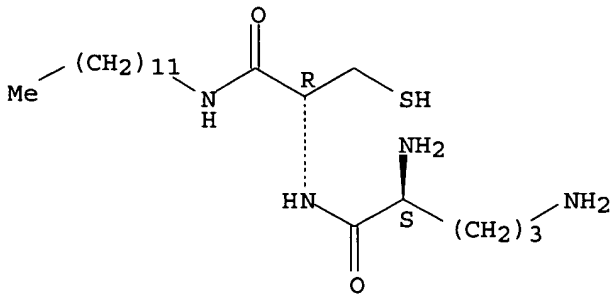


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L40 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **227176-24-1** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-dodecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C20 H42 N4 O2 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal; Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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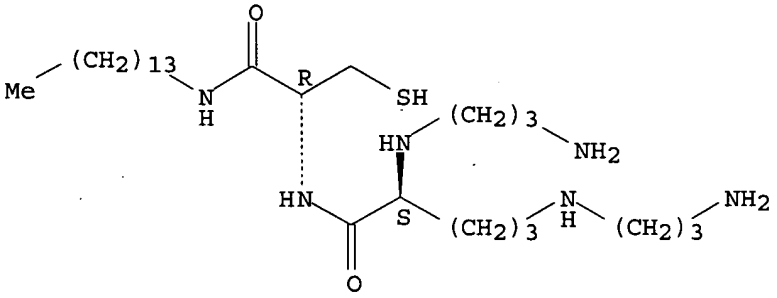
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide l53 tot

L53 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN **361525-75-9** REGISTRY
CN L-Cysteinamide, N2,N5-bis(3-aminopropyl)-L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H60 N6 O2 S
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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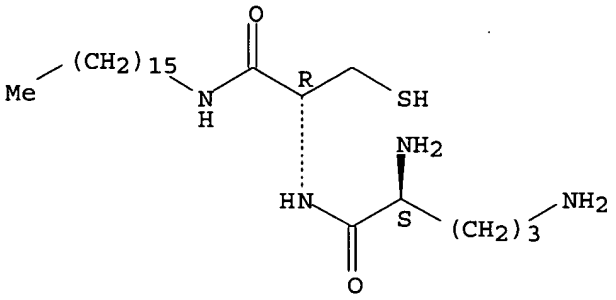
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L53 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN **361525-74-8** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-hexadecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H50 N4 O2 S
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.



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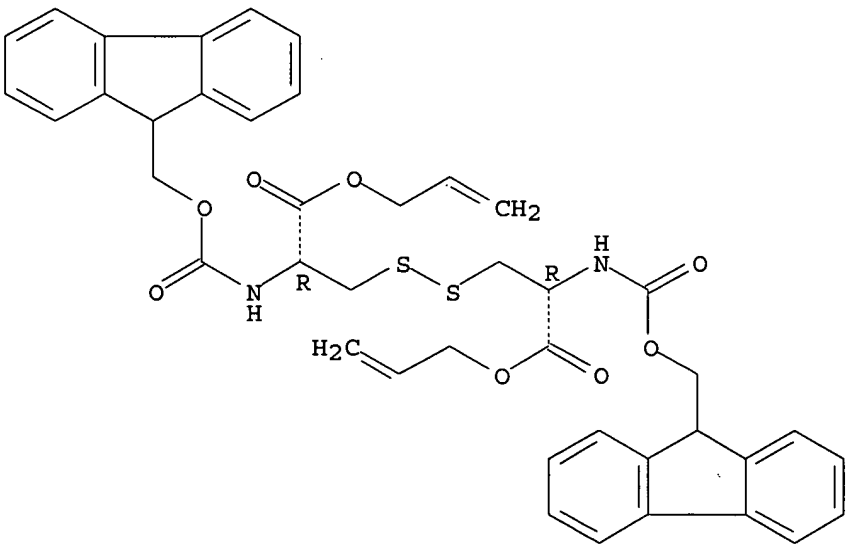
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L53 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN **361525-73-7** REGISTRY
CN L-Cystine, N,N'-bis[(9H-fluoren-9-ylmethoxy)carbonyl]-, di-2-propenyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H40 N2 O8 S2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



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L53 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN **227176-25-2** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H46 N4 O2 S
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Conference; Journal; Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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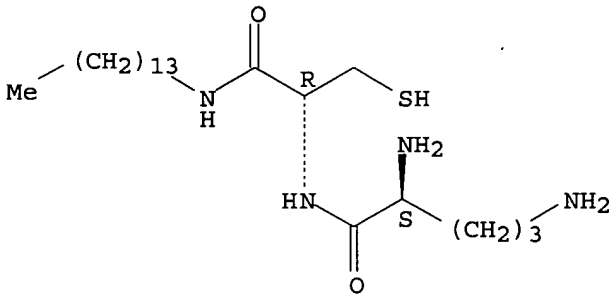
Absolute stereochemistry.



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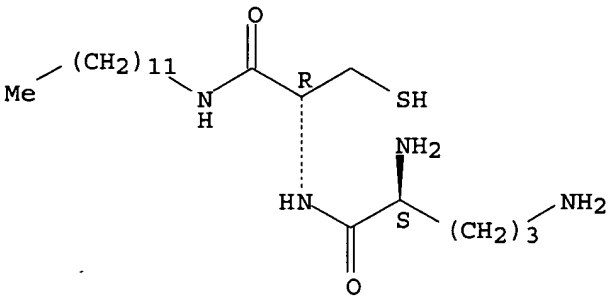
8 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L53 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN **227176-24-1** REGISTRY
CN L-Cysteinamide, L-ornithyl-N-dodecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H42 N4 O2 S
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal; Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L2   (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND PROPANAMIDE
L3   (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  C18H38N4O2S/MF
L4   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND CYSTEINAMIDE
L5             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L4
L6               STR
L7               SCR 2021
L8               SCR 2039 OR 2050 OR 2049 OR 2053 OR 2043 OR 2054
L9               SCR 1771
L10  (    100150)SEA FILE=REGISTRY SSS FUL L6 AND L7 AND L9 NOT L8
L11              STR
L12         1065 SEA FILE=REGISTRY SUB=L10 CSS FUL L11

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L14  (       167)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("BEHR J"/AU OR "BEHR J P"/AU
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L16  (       461)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("WAGNER ERNST"/AU OR "WAGNER
L17  (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SCHUELLER S"/AU
L18  (      3663)SEA FILE=HCAPLUS ABB=ON  PLU=ON  UNIVERSITE LOUIS PASTEUR?/CS,P
L19  (      3289)SEA FILE=HCAPLUS ABB=ON  PLU=ON  BOEHRINGER INGELHEIM?/CS,PA
L20           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR L
L21            4 L5
L22            4 L21 AND L14-17
L23            4 L21 AND L18-19
L24         1191 L13 (L) RACT+NT/RL
L25            4 L24 AND L14-17
L26            7 L24 AND L18-19
L27         1187 L24 NOT L25
L28          892 L27 AND (PY<=1998 OR AY<=1998 OR PRY<=1998 OR PD<19981128 OR AD
L29       657989 NUCLEIC ACIDS+OLD,NT/CT
L30         5241 NUCLEIC ACID LIBRARY+NT/CT
L31         9067 COMBINATORIAL LIBRARY+NT/CT
L32           65 CHEMICAL LIBRARY/CT
L33        84991 NUCLEOSIDES+OLD,NT/CT
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L34      288337 NUCLEOTIDES+NT/CT
L35          33 L28 AND L29-34

     FILE 'REGISTRY' ENTERED AT 15:00:47 ON 09 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 15:00:51 ON 09 JUN 2004
L36             TRA L20 1- RN :       45 TERMS

     FILE 'REGISTRY' ENTERED AT 15:00:51 ON 09 JUN 2004
L37          45 SEA L36
L38           5 L12 AND L37
L39           8 L37 AND S/ELS
L40           4 L39 AND (C28 H60 N6 O2 S OR C24 H50 N4 O2 S OR C22 H46 N4 O2 S
L41           0 C24 H50 N4 O2 S
L42           1 C24H50N4O2S
L43           1 C22H46N4O2S
L44           3 C20H42N4O2S
L45           1 C28H60N6O2S
                SEL RN L40
L46           0 E1-4/CRN

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L47           8 L40
L48           8 L47 AND L14-17
L49           7 L47 AND L18-19
L50           2 L35 AND (PHOTOCHEMICAL REDUCTION OR DEHALOGENATION)/TI

     FILE 'REGISTRY' ENTERED AT 17:01:38 ON 09 JUN 2004
L51           4 227176-25-2 OR 227176-24-1 OR 361525-74-8 OR 361525-75-9
L52           1 361525-73-7
L53           5 L51-52

     FILE 'HCAPLUS' ENTERED AT 17:10:09 ON 09 JUN 2004
L54           8 L53
L55           8 L54 AND L14-17
L56           7 L54 AND L18-19

=> b hcap
FILE 'HCAPLUS' ENTERED AT 17:11:47 ON 09 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 9 Jun 2004  VOL 140 ISS 24
FILE LAST UPDATED: 8 Jun 2004  (20040608/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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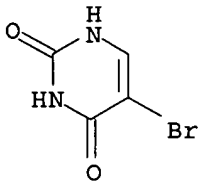
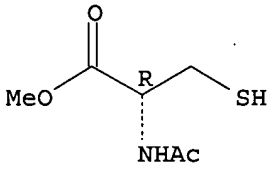
L50 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:633512 HCAPLUS
DN 111:233512
ED Entered STN: 23 Dec 1989
TI **Photochemical reduction** of 5-bromouracil by cysteine derivatives and coupling of 5-bromouracil to cystine derivatives
AU Dietz, Timothy M.; Koch, Tad H.
CS Dep. Chem. Biochem., Univ. Colorado, Boulder, CO, 80309-0215, USA
SO Photochemistry and Photobiology (**1989**), 49(2), 121-9
CODEN: PHCBAP; ISSN: 0031-8655
DT Journal
LA English
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 33
AB Irradiation of pH 7, aqueous solns. of 5-bromouracil (I) in the presence of cysteine peptide-like derivs., e.g. Ac-Cys-OMe, at 308 nm using a XeCl excimer laser yielded initial formation of only uracil and the corresponding cystine derivative Continued irradiation yielded an S-uracilylcysteinyl adduct as well as addnl. uracil and cystine derivative Similar irradiation of a solution of I and a cystine derivative yielded initial formation of uracil and the S-uracilylcysteinyl adduct. Formation of these products as well as secondary products of uracil photochem. was observed upon irradiation of the resp. solns. with 254 nm light. With 308 nm laser excitation, uracil-cysteine adduct formation and reduction of I to uracil occur via initial electron transfer from the disulfide of the cysteine derivative to triplet I. The quantum yield of I destruction with 308 nm excitation in the presence of cysteine derivative is 1.1 + 10-3. Reaction of triplet I with the cysteine derivative does not yield uracil-cysteine adduct but uracil and cystine derivative
ST photochem coupling bromouracil cystine cysteine; cysteine photochem redn bromouracil
IT Reduction, photochemical
(of bromouracil with cysteine derivs.)
IT Coupling reaction
(photochem., of bromouracil with cysteine and cystine derivs.)
IT 616-91-1, N-Acetylcysteine
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)
IT 66-22-8P, Uracil, preparation
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, by photochem. reduction of bromouracil in presence of cysteine derivs.)
IT **51-20-7**, 5-Bromouracil
RL: RCT (Reactant); RACT (Reactant or reagent)
(photochem. reduction and coupling reaction of, with cysteine and cystine derivs.)
IT 123798-62-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and photochem. coupling reaction of, with bromouracil)
IT 66127-81-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and photochem. oxidation-dimerization and coupling reaction of, with bromouracil)
IT 32381-28-5P 123798-63-0P 123798-64-1P
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
IT **7652-46-2P**, N-Acetylcysteine methyl ester
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation, aminolysis, and photochem. oxidation-dimerization and coupling reaction of, with bromouracil)
IT **51-20-7**, 5-Bromouracil
RL: RCT (Reactant); RACT (Reactant or reagent)
(photochem. reduction and coupling reaction of, with cysteine and cystine derivs.)
RN 51-20-7 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo- (9CI) (CA INDEX NAME)

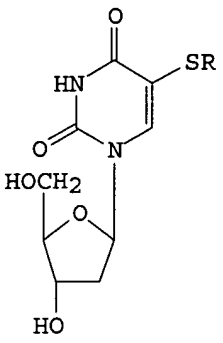


IT **7652-46-2P**, N-Acetylcysteine methyl ester
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation, aminolysis, and photochem. oxidation-dimerization and coupling reaction of, with bromouracil)
RN 7652-46-2 HCAPLUS
CN L-Cysteine, N-acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L50 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1978:615691 HCAPLUS
DN 89:215691
ED Entered STN: 12 May 1984
TI Formation of S-[5-(2'-deoxyuridyl)]thiol compounds in the **dehalogenation** of 5-bromo- and 5-iodo-2'-deoxyuridine with cysteine derivatives
AU Chikuma, Toshiyuki; Negishi, Kazuo; Hayatsu, Hikoya
CS Fac. Pharm. Sci., Univ. Tokyo, Tokyo, Japan
SO Chemical & Pharmaceutical Bulletin (**1978**), 26(6), 1746-52
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
CC 33-7 (Carbohydrates)
Section cross-reference(s): 28, 34
GI



VIII

AB Dehalogenations of 5-bromo- (I) and 5-iodo-2'-deoxyuridine (II) by RSH in aqueous solns. were studied. The thiols used were cysteine (III), and its Me and Et (IV) esters, cysteamine (V), homocysteine (VI), glutathione (VII), 2-mercaptoethanol, and 2-mercaptopropionic acid. The products VIII, and the rate consts. were determined At pH 8 and 37°, the dehalogenation rates by these thiols decreased in the above-mentioned order. 5-Alkyluracil derivs. were formed in the reaction between I and III - VII, as well as in the reaction between II and III. This indicated that the SN2 mechanism proposed by Y. Wataya, K. Negishi and H. Hayatsu, (1973) is generally operating in these dehalogenations.

ST dehalogenation halodeoxyuridine; thiouridine; uridine halodeoxy thiol reaction; cysteine halodeoxyuridine reaction

IT Dehalogenation
(of 5-halo-2'-deoxyuridines by thiol)

IT Kinetics of dehalogenation
(of 5-halo-2'-deoxyuridines with cysteine derivs.)

IT **Nucleosides, reactions**
(2'-deoxy-5-halo-, reaction of, with cysteine derivs.)

IT 67797-20-0P 68418-79-1P 68418-80-4P 68418-81-5P 68418-82-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 52-90-4, reactions 60-23-1 60-24-2 70-18-8, reactions 79-42-5 **2485-62-3 3411-58-3** 6027-13-0
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(reaction of, with 5-halo-2'-deoxyuridines)

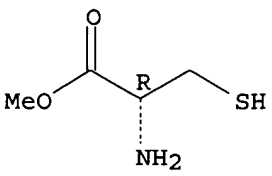
IT **54-42-2 59-14-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thiol)

IT **2485-62-3 3411-58-3**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(reaction of, with 5-halo-2'-deoxyuridines)

RN 2485-62-3 HCAPLUS

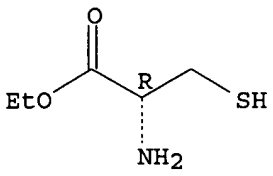
CN L-Cysteine, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



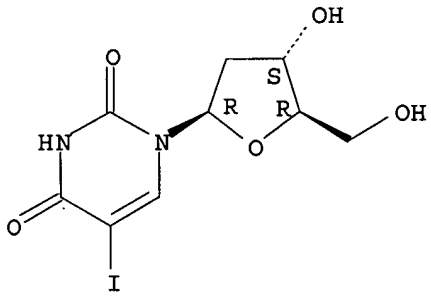
RN 3411-58-3 HCAPLUS
CN L-Cysteine, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



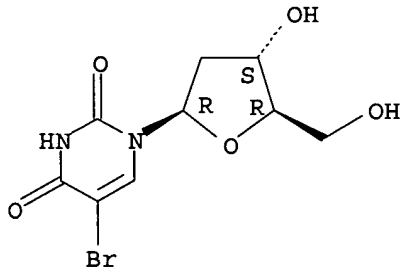
IT **54-42-2 59-14-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thiol)
RN 54-42-2 HCAPLUS
CN Uridine, 2'-deoxy-5-iodo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 59-14-3 HCAPLUS
CN Uridine, 5-bromo-2'-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L2   (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND PROPANAMIDE
L3   (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  C18H38N4O2S/MF
L4   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND CYSTEINAMIDE
L5             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L4
L6               STR
L7               SCR 2021
L8               SCR 2039 OR 2050 OR 2049 OR 2053 OR 2043 OR 2054
L9               SCR 1771
L10  (    100150)SEA FILE=REGISTRY SSS FUL L6 AND L7 AND L9 NOT L8
L11              STR
L12         1065 SEA FILE=REGISTRY SUB=L10 CSS FUL L11

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L13         2193 L12
                 ACT SCHNHCAP/A
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L15  (         10)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("BLESSING T"/AU OR "BLESSING
L16  (        461)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("WAGNER ERNST"/AU OR "WAGNER
L17  (          2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SCHUELLER S"/AU
L18  (       3663)SEA FILE=HCAPLUS ABB=ON  PLU=ON  UNIVERSITE LOUIS PASTEUR?/CS,P
L19  (       3289)SEA FILE=HCAPLUS ABB=ON  PLU=ON  BOEHRINGER INGELHEIM?/CS,PA
L20            11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR L
L21             4 L5
L22             4 L21 AND L14-17
L23             4 L21 AND L18-19
L24          1191 L13 (L) RACT+NT/RL
L25             4 L24 AND L14-17
L26             7 L24 AND L18-19
L27          1187 L24 NOT L25
L28           892 L27 AND (PY<=1998 OR AY<=1998 OR PRY<=1998 OR PD<19981128 OR AD
L29        657989 NUCLEIC ACIDS+OLD,NT/CT
L30          5241 NUCLEIC ACID LIBRARY+NT/CT
L31          9067 COMBINATORIAL LIBRARY+NT/CT
L32            65 CHEMICAL LIBRARY/CT
L33         84991 NUCLEOSIDES+OLD,NT/CT
L34        288337 NUCLEOTIDES+NT/CT
L35            33 L28 AND L29-34

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L36              TRA L20 1- RN :       45 TERMS

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L37            45 SEA L36
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L39             8 L37 AND S/ELS
L40             4 L39 AND (C28 H60 N6 O2 S OR C24 H50 N4 O2 S OR C22 H46 N4 O2 S
L41             0 C24 H50 N4 O2 S
L42             1 C24H50N4O2S
L43             1 C22H46N4O2S
L44             3 C20H42N4O2S
L45             1 C28H60N6O2S
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L49             7 L47 AND L18-19
L50             2 L35 AND (PHOTOCHEMICAL REDUCTION OR DEHALOGENATION)/TI

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L51             4 227176-25-2 OR 227176-24-1 OR 361525-74-8 OR 361525-75-9
L52             1 361525-73-7
L53             5 L51-52

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L54             8 L53
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L56             7 L54 AND L18-19
L57             8 L47 OR L54

=> b hcap
FILE 'HCAPLUS' ENTERED AT 17:36:18 ON 09 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 9 Jun 2004  VOL 140 ISS 24
FILE LAST UPDATED: 8 Jun 2004  (20040608/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L57  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:283734  HCAPLUS
DN   139:64018
ED   Entered STN:  13 Apr 2003
TI   Monomolecular condensation of DNA by cationic detergents
AU   Dauty, Emmanuel; Behr, Jean-Paul
CS   Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de
     Strasbourg, Faculte de Pharmacie BP 24, Illkirch, 67401, Fr.
SO   Polymer International (2003), 52(4), 459-464
     CODEN: PLYIEI; ISSN: 0959-8103
PB   John Wiley & Sons Ltd.
DT   Journal
LA   English
CC   3-2 (Biochemical Genetics)
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Section cross-reference(s): 6

AB Controlling the size of condensed DNA particles is a key determinant for their diffusion in vivo as well as for gene delivery to target cells. Towards this goal, DNA mols. were compacted individually by cationic thiol-detergents into discrete nanometric entities. These particles were then stabilized by air-induced dimerization of the detergent into a disulfide lipid on the template DNA. Using a tetradecane-cysteine-ornithine (C14COrn) detergent, a solution of 5.5 Kb plasmid DNA was thus converted into a monodisperse population of 35-nm particles. The stability of the complexes, as well as their size, morphol. and transfection efficiencies were investigated. Surprisingly, the electrophoretic mobility of the quasi-neutral condensed DNA was found higher than that of the extended DNA polyanion. The diams. of particles resulting from the condensation of DNA of various sizes was measured by dynamic light scattering and found to vary as the cubic root of the DNA size. In an attempt to extend their biodistribution and to target tumor cells, we have prepared folate-poly(ethylene oxide)-coated particles that were shown to bind to the cell-surface folate receptor.

ST DNA condensation diffusion cationic detergent particle gene delivery

IT Polyoxyalkylenes, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(3400; monomol. condensation of DNA by cationic detergents)

IT Conformation
(DNA, condensation and diffusion; monomol. condensation of DNA by cationic detergents)

IT Animal cell line
(KB, gene delivery to; monomol. condensation of DNA by cationic detergents)

IT Detergents
(cationic; monomol. condensation of DNA by cationic detergents)

IT Lipids, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cationic; monomol. condensation of DNA by cationic detergents)

IT DNA
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(complexes, detergents with; monomol. condensation of DNA by cationic detergents)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(folate, cells binding by; monomol. condensation of DNA by cationic detergents)

IT Liver
(hepatocyte, transformation; monomol. condensation of DNA by cationic detergents)

IT Polyoxyalkylenes, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lipid-folate conjugates; monomol. condensation of DNA by cationic detergents)

IT Molecular association
Transformation, genetic
(monomol. condensation of DNA by cationic detergents)

IT Plasmids
(pCMV-Luc; monomol. condensation of DNA by cationic detergents)

IT 25322-68-3, PEG
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(3400; monomol. condensation of DNA by cationic detergents)
IT **227176-25-2**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(complexes with DNA; monomol. condensation of DNA by cationic detergents)
IT 25322-68-3D, PEG, lipid-folate conjugates 628732-60-5
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monomol. condensation of DNA by cationic detergents)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Allen, T; Biochim Biophys Acta 1991, V1066, P29 HCAPLUS
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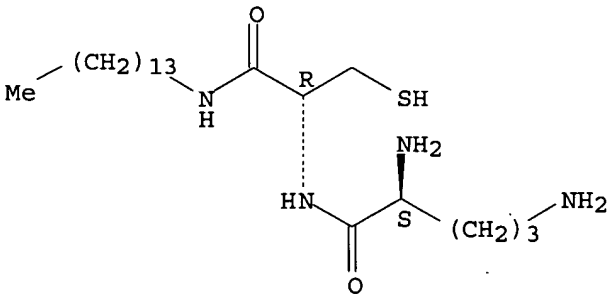
IT **227176-25-2**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(complexes with DNA; monomol. condensation of DNA by cationic detergents)
RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:880495 HCAPLUS
DN 138:112108
ED Entered STN: 21 Nov 2002
TI Investigation of the stability of dimeric cationic surfactant/DNA complexes and their interaction with model membrane systems
AU Lleres, David; Clamme, Jean-Pierre; Dauty, Emmanuel; Blessing, Thomas;

Krishnamoorthy, Guruswamy; Duportail, Guy; Mely, Yves
CS Laboratoire de Pharmacologie et Physicochimie des Interactions Cellulaires et Moleculaires, Faculte de Pharmacie Universite Louis Pasteur, Illkirch, 67401, Fr.
SO Langmuir (2002), 18(26), 10340-10347
CODEN: LANGD5; ISSN: 0743-7463
PB American Chemical Society
DT Journal
LA English
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1, 3, 6
AB The stability of the complexes between DNA and nonviral vectors is a crucial parameter for efficient gene delivery into target cells. The stability must be high enough to prevent any dissociation during interaction with the plasma membrane but low enough to allow the dissociation that is required for efficient internalization into the nucleus. The authors investigated the stability of complexes of DNA with two cysteine surfactants (guanidinocysteine N-decylamide, C10-CG+, and ornithinyl-cysteinyl-tetradecylamide, C14-CO), able to convert themselves, via oxidative dimerization, into cationic cystine lipids. To this end, the authors determined the critical aggregation concentration (cac) and the binding consts. of the surfactants for DNA by using the fluorescence quenching of the DNA bis-intercalating agent, YOYO-1, that results from the dye clustering induced by the collapse of DNA. The cac's of C10-CG+ and C14-CO monomeric forms are 2.5 and 1 μM, resp., and are slightly less than the 5 μM value for CTAB, taken as a model of nondimerizable surfactant. Dimerization of C10-CG+ and C14-CO reduces the cac to 400 and 1 nM, resp. The strong stabilization induced by oxidation of C14-CO is further confirmed by the increase in the rigidity of the micellelike domains in the complexes, as deduced from the rotational correlation time of the hydrophobic probe 1,6-diphenylhexatriene. In keeping with the stability data, no dissociation of the (C14-CO)2/DNA complexes occurs in the presence of neutral vesicles (that mimic the external leaflet of the plasma membrane), while a significant dissociation was observed with (C10-CG+)2/DNA complexes and an even larger one with CTAB/DNA complexes. Similarly, (C14-CO)2/DNA complexes do not dissociate in the presence of anionic vesicles (that mimic the cytoplasmic leaflet of the plasma membrane), while a complete dissociation and DNA release occurs with both (C10-CG+)2/DNA and CTAB/DNA complexes. Both the initial interaction with the plasma membrane and the release of DNA in the cytoplasm are strongly dependent on the stability of the complexes obtained with this new class of nonviral vectors.
ST cationic surfactant dimer DNA complex stability interaction membrane
IT DNA
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(complexes, with cationic surfactant monomers and dimers; stability of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT Aggregation
Critical micelle concentration
(critical aggregation and micellization concentration of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT Phosphatidylcholines, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)

(membrane; stability of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT Membrane, biological
(phosphatidylcholine; stability of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT Free energy of binding
Molecular association
(stability of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT 1239-45-8, Ethidium bromide 143413-85-8, YOYO-1
RL: NUU (Other use, unclassified); USES (Uses)
(reporter dye; critical aggregation and micellization concentration of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
IT 57-09-0D, Cetyltrimethylammonium bromide, complexes with DNA
213468-24-7D, complexes with DNA 227176-10-5D, complexes with DNA
227176-25-2D, complexes with DNA 486430-00-6D, complexes with DNA
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(stability of DNA complexes with cationic surfactants and CTAB and interaction with model membrane systems)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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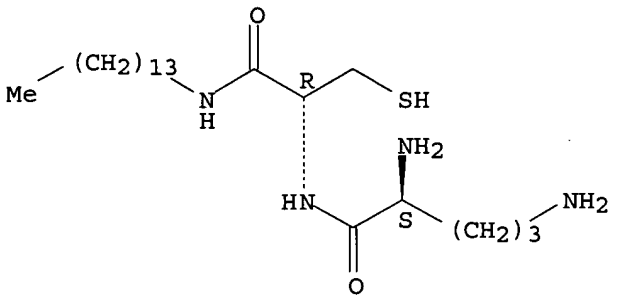
IT **227176-25-2D**, complexes with DNA
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(stability of DNA complexes with cationic surfactants and CTAB and

interaction with model membrane systems)
RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:457871 HCAPLUS
DN 137:174731
ED Entered STN: 19 Jun 2002
TI Intracellular Delivery of Nanometric DNA Particles via the Folate Receptor
AU Dauty, Emmanuel; Remy, Jean-Serge; Zuber, Guy; Behr, Jean-Paul
CS Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de Strasbourg Faculte de Pharmacie BP 24, CNRS/Universite Louis Pasteur de Strasbourg, Illkirch, 67401, Fr.
SO Bioconjugate Chemistry (2002), 13(4), 831-839
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB The size of condensed DNA particles is a key determinant for both diffusion to target cells in vivo and intracellular trafficking. The smallest complexes are obtained when each DNA mol. collapses individually. This was achieved using a designed cationic thiol-detergent, tetradecyl-cysteinyl-ornithine (C14COrn). The resulting particles were subsequently stabilized by air-induced dimerization of the detergent into a disulfide lipid on the DNA template. Particles are anionic (zeta potential = -45 mV), and their size (30 nm) corresponds to the volume of a single plasmid DNA mol. The electrophoretic mobility of the condensed DNA, though quasi-neutralized, was found higher than that of the extended DNA. Moreover, the dimerized (C14COrn)2 lipid was found to be an efficient transfection reagent for various cell lines. In an attempt to achieve extended circulation times and to target tumors by systemic delivery, we have coated the particles with PEG-folate residues. Plasmid DNA was condensed into monomol. particles as described above and coated by simple mixing with DPPE-PEG-folate. Physicochem. measurements showed particles coated with 2% of DPPE-PEG3400-folate remain monomol. and are stable in the cell-culture medium. Caveolae-mediated cell entry was demonstrated by ligand-dependence, by competition with excess folic acid as well as by confocal microscopy.
ST DNA intracellular delivery folate receptor
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(folate; intracellular delivery of nanometric DNA particles via the folate receptor)

IT Genetic vectors
Particle size
Transformation, genetic
(intracellular delivery of nanometric DNA particles via the folate receptor)
IT DNA
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(intracellular delivery of nanometric DNA particles via the folate receptor)
IT 59-30-3, Folic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intracellular delivery of nanometric DNA particles via the folate receptor)
IT 126111-99-7DP, complexes with DNA and tetradecylornithinylcysteine
227176-25-2DP, complexes with DNA
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intracellular delivery of nanometric DNA particles via the folate receptor)
IT 5681-36-7, DPPE 126111-99-7 153999-73-6 **227176-25-2**
357277-60-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(intracellular delivery of nanometric DNA particles via the folate receptor)
IT 448963-52-8DP, folate-conjugates 448963-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intracellular delivery of nanometric DNA particles via the folate receptor)
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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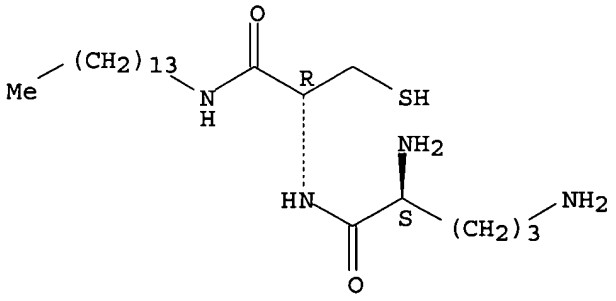
IT **227176-25-2DP**, complexes with DNA
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intracellular delivery of nanometric DNA particles via the folate receptor)

RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

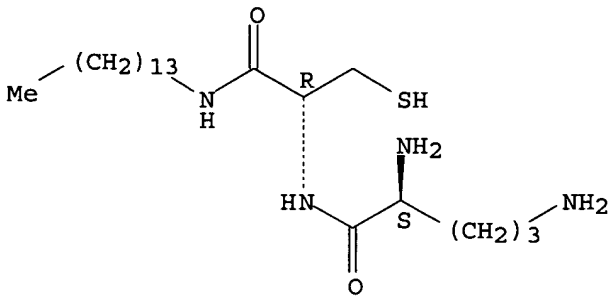
Absolute stereochemistry.



IT **227176-25-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(intracellular delivery of nanometric DNA particles via the folate receptor)

RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:405503 HCAPLUS
DN 138:126858
ED Entered STN: 30 May 2002
TI Development of plasmid and oligonucleotide nanometric particles
AU Dauty, E.; Behr, J.-P.; Remy, J.-S.
CS Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de Strasbourg, Faculte de Pharmacie, Illkirch, 67401, Fr.
SO Gene Therapy (2002), 9(11), 743-748
CODEN: GETHEC; ISSN: 0969-7128
PB Nature Publishing Group
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
AB Nucleic acids delivery vectors have shown promising therapeutic potential in model systems. However, comparable clin. success is delayed essentially because of their poor biodistribution and of their ineffective intracellular trafficking. The size of condensed DNA particles is a key determinant for in vivo diffusion, as well as for gene delivery to the cell nucleus. Towards this goal, we have developed cationic thiol-detergents that individually compact plasmid DNA mols. into anionic particles. These particles are then "stabilized" by air-induced dimerization of the detergent into a disulfide lipid on the template DNA. The particles all measure approx. 30 nm, which corresponds to the volume of a single mol. of plasmid DNA. The gel electrophoretic mobility of the anionic particles was found to be higher than that of the plasmid DNA itself. Similarly, particles formed with a 31-mer oligonucleotide measured 19 nm. Improved in vivo diffusion, as well as improved intracellular trafficking may be inferred from the faster migration of the complexes. Moreover, the size of the particles remains compatible with nuclear pore crossing. Finally, in an attempt to improve the biodistribution of these particles, we have coated the monomol. particles with a poly(ethylene glycol) corona.
ST cationic thiol detergent plasmid DNA transfection; oligonucleotide cationic thiol detergent nanoparticle gene delivery
IT DNA
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(complexes; plasmid and oligonucleotide nanometric particles for gene delivery)
IT Genetic vectors
Plasmid vectors
Transformation, genetic

(plasmid and oligonucleotide nanometric particles for gene delivery)
IT Oligodeoxyribonucleotides
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(plasmid and oligonucleotide nanometric particles for gene delivery)
IT Detergents
(thiol, cationic; plasmid and oligonucleotide nanometric particles for gene delivery)
IT 145035-97-8, DPPE-PEG **227176-25-2 361525-74-8 361525-75-9**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(plasmid and oligonucleotide nanometric particles for gene delivery)
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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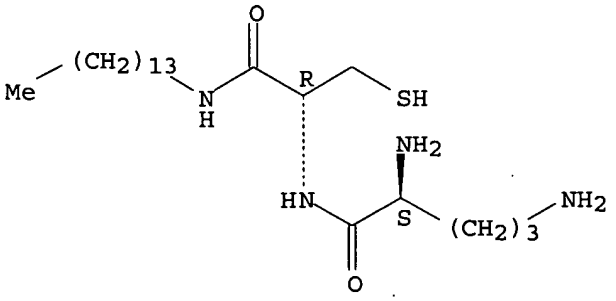
(19) Zanta, M; Bioconj Chem 1997, V8, P839 HCAPLUS
IT **227176-25-2 361525-74-8 361525-75-9**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(plasmid and oligonucleotide nanometric particles for gene delivery)
RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

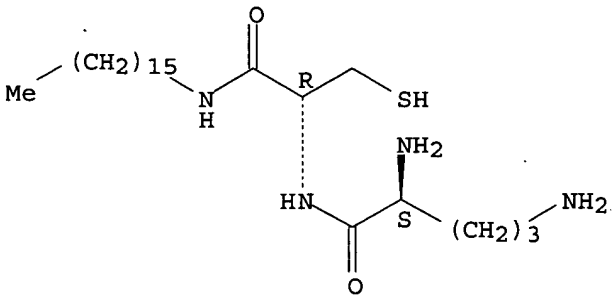
Absolute stereochemistry.



RN 361525-74-8 HCAPLUS

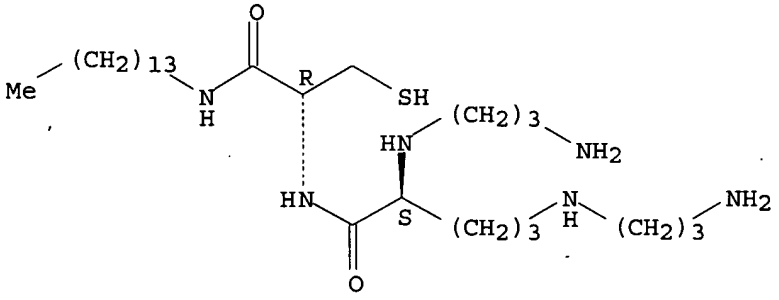
CN L-Cysteinamide, L-ornithyl-N-hexadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 361525-75-9 HCAPLUS
CN L-Cysteinamide, N2,N5-bis(3-aminopropyl)-L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:350540 HCAPLUS
DN 138:112277
ED Entered STN: 10 May 2002
TI Dimerizable cationic detergents condense plasmid DNA into 30 nm particles and transfect cells in vitro
AU Dauty, E.; Remy, J. S.; Blessing, T.; Behr, J. P.
CS Faculte de Pharmacie de Strasbourg, Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur, Illkirch, 67401, Fr.
SO Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1135-1136
Publisher: Controlled Release Society, Minneapolis, Minn.
CODEN: 69CNY8
DT Conference
LA English
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
AB In the present investigation, we reported the biophys. and biol. properties of the ornithinylcysteinyltetradecylamide (C14COrn). This new dimerizable detergent condenses plasmid DNA into monomol. particles of 30 nm. This complexes are mobile in agarose gel and exhibit a typical lipid/DNA supramol. structure. When the complexes are large and cationic

they show a transfection efficiency comparable to that obtained with the most potent vectors.
ST dimer cationic detergent plasmid DNA transfection
IT Detergents
(cationic; dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
IT DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
IT Drug delivery systems
Gene therapy
Transformation, genetic
(dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
IT DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
IT **227176-25-2D**, DNA complexes
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detergent; dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Behr, J; Tet Letters 1986, V27, P5861 HCAPLUS
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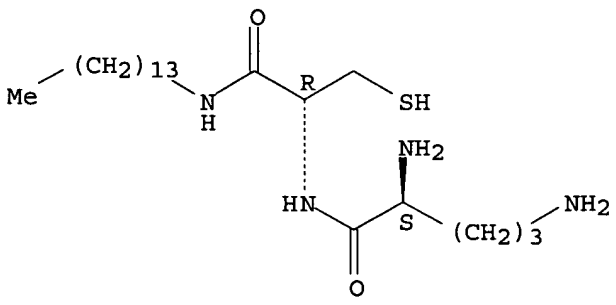
(4) Labatmoleur, F; Gene Ther 1996, V3, P1010 HCAPLUS
(5) Melnikov, S; J Am Chem Soc 1995, V117, P2401 HCAPLUS
(6) Zanta, M; Bioconjuguate Chem 1997, V8, P839 HCAPLUS
IT **227176-25-2D**, DNA complexes
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detergent; dimerizable cationic detergents condense plasmid DNA into 30-nm particles and transfect cells)
RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:636468 HCAPLUS
DN 135:252520
ED Entered STN: 02 Sep 2001

TI Dimerizable Cationic Detergents with a Low cmc Condense Plasmid DNA into Nanometric Particles and Transfect Cells in Culture
AU Dauty, Emmanuel; Remy, Jean-Serge; Blessing, Thomas; Behr, Jean-Paul
CS Laboratoire de Chimie Genetique, CNRS/Universite Louis Pasteur de Strasbourg Faculte de Pharmacie, Illkirch, 67401, Fr.
SO Journal of the American Chemical Society (2001), 123(38), 9227-9234
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 9, 26, 63
AB The size of condensed DNA particles is a key determinant for in vivo diffusion and gene delivery to cells. Gene mols. can be individually compacted by cationic thiol detergents into nanometric particles that are stabilized by oxidative conversion of the detergent into a gemini lipid. To reach the other goal, gene delivery, a series of cationic thiol detergents with various chain lengths (C12-C16) and headgroups (ornithine or spermine) was prepared, using a versatile polymer-supported synthetic strategy. Critical micelle concns. and thiol oxidation rates of the detergents were measured. The formation and stability of complexes formed with plasmid DNA, as well as the size, ξ-potential, morphol., and transfection efficiency of the particles were investigated. Using the tetradecane/ornithine detergent, a solution of 5.5 Kpb plasmid DNA mols. was converted into a homogeneous population of 35 nm particles. The same detergent, once oxidized, exhibited a typical lipid phase internal structure and was capable of effective cell transfection. The particle size did not increase with time. Surprisingly, the gel electrophoretic mobility of the DNA complexes was found to be higher than that of plasmid DNA itself. Favorable in vivo diffusion and intracellular trafficking properties may thus be expected for these complexes.
ST transfection nanometric particle plasmid DNA tetradecane ornithine detergent; detergent cationic thiol cmc oxidn plasmid DNA complex transfection
IT Molecular association
((C14COrn)/DNA complexes; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(closed circular; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)
IT Critical micelle concentration
Nanoparticles
Particle shape
Solid phase synthesis
Transformation, genetic
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)
IT Particle size
(nanoscale; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)
IT Plasmids
(pCMV-luc; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)
IT Bond formation
(sulfur-sulfur; dimerizable cationic detergents with a low cmc condense

plasmid DNA into nanometric particles and transfect cells in culture)

IT 173966-44-4DP, bead-grafted **361525-73-7P**
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

IT 70-26-8, Ornithine 124-22-1, Dodecylamine 143-27-1, Hexadecylamine 2016-42-4, Tetradecylamine 142601-71-6 186002-24-4 362046-48-8D, NovaSyn MMT alcohol resin, PEG derivative
RL: RCT (Reactant); RACT (Reactant or reagent)
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

IT **227176-25-2P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

IT **227176-24-1P 361525-74-8P 361525-75-9P**
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

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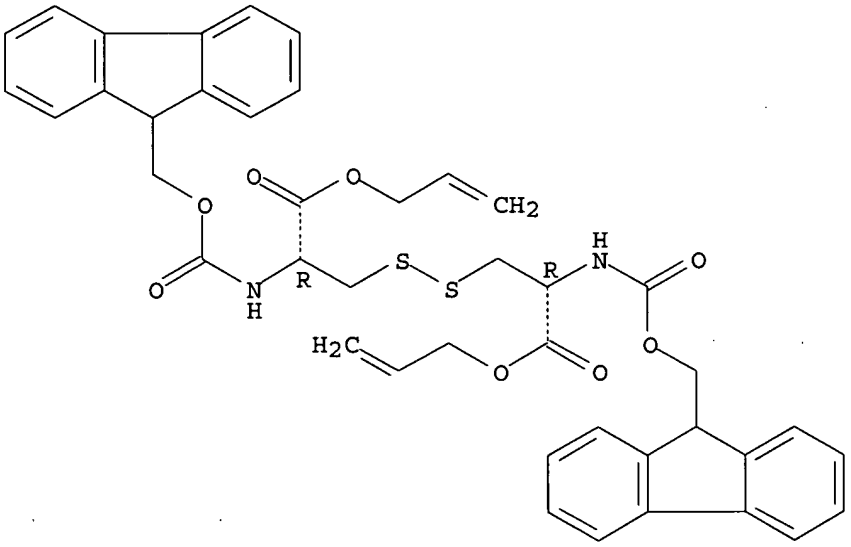
IT **361525-73-7P**
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

RN 361525-73-7 HCAPLUS

CN L-Cystine, N,N'-bis[(9H-fluoren-9-ylmethoxy)carbonyl]-, di-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



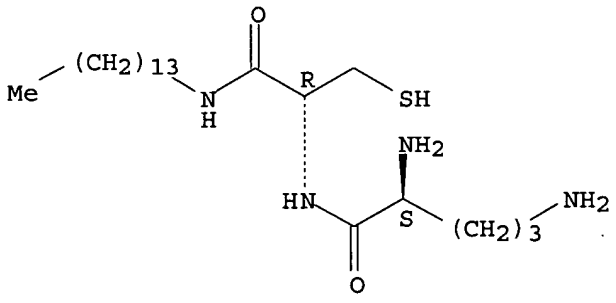
IT **227176-25-2P**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

RN 227176-25-2 HCAPLUS

CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



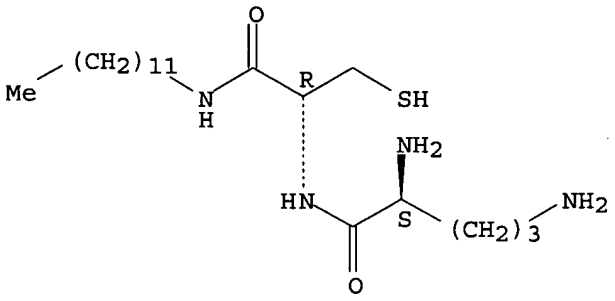
IT **227176-24-1P 361525-74-8P 361525-75-9P**

RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

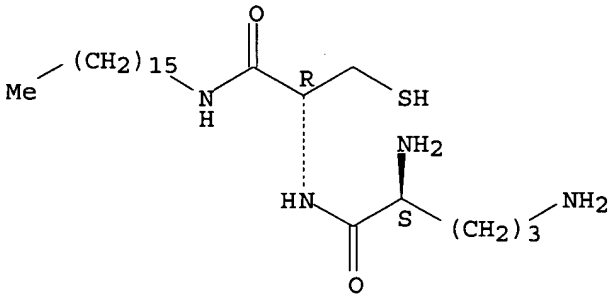
RN 227176-24-1 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-dodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



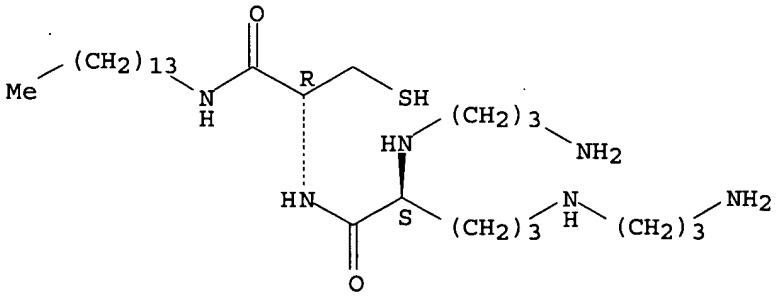
RN 361525-74-8 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-hexadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 361525-75-9 HCAPLUS
CN L-Cysteinamide, N2,N5-bis(3-aminopropyl)-L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:483530 HCAPLUS
DN 136:195946
ED Entered STN: 05 Jul 2001
TI DNA condensation by an oxidizable cationic detergent. Interactions with lipid vesicles
AU Lleres, D.; Dauty, E.; Behr, J.-P.; Mely, Y.; Duportail, G.
CS UMR 7034 du CNRS, Laboratoire de Pharmacologie et Physicochimie des Interactions Cellulaires et Moleculaires, Illkirch, 67401, Fr.
SO Chemistry and Physics of Lipids (2001), 111(1), 59-71
CODEN: CPLIA4; ISSN: 0009-3084
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 6-7 (General Biochemistry)
Section cross-reference(s): 3
AB Cationic amphiphile-mediated delivery of plasmid DNA is the non-viral gene transfer method most often used. In the present work, we considered a new cysteine-detergent, ornithinyl-cysteinyl-tetradecylamide (C14-CO), able to convert itself, via oxidative dimerization, into a cationic cystine-lipid. By using fluorescence techniques, we first characterized the structure of complexes of plasmid DNA with C14-CO mols. either kept as monomers, or oxidized into dimers. Both forms are able to condense DNA, with the formation of hydrophobic micelle-like domains along the DNA chain. Domains with a larger mol. order were obtained with dimeric C14-CO/DNA complexes. In a second step, the interactions of these complexes with lipid vesicles considered as membrane models were investigated. In the presence of vesicles, we observed a decondensation of the DNA involved in complexes obtained with C14-CO monomers. With anionic vesicles, the DNA is released into the bulk solution, while with neutral vesicles, it remains bound to the vesicles via electrostatic interactions with inserted C14-CO mols. In sharp contrast, the complexes with C14-CO dimers are unaffected by the addition of either neutral or anionic vesicles and show no interaction with them. These results may partly explain the low transfection efficiency of these complexes at the ± charge ratios used in this study.
ST DNA condensation cysteine detergent cationic cystine lipid vesicle interaction
IT Disulfide group
(C14-CO dimer; DNA condensation by an oxidizable cationic detergent (C14-CO) and interactions of DNA/detergent complexes with lipid vesicles)
IT Fluorescent indicators
Hydrophobicity
Molecular association
(DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT Conformation
(DNA; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT Electrostatic force
(attractive; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT Detergents
(cationic; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT DNA
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(closed circular; DNA condensation by an oxidizable cationic detergent

and interactions of DNA/detergent complexes with lipid vesicles)
IT Phosphatidylcholines, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complexes, with monomeric (reduced) C14-CO/DNA; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT DNA
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(complexes; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT Attractive force
(electrostatic; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT Liposomes
(large unilamellar; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT **227176-25-2**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(C14-CO; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
IT 1720-32-7, 1,6-Diphenylhexatriene
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(fluorescent probe; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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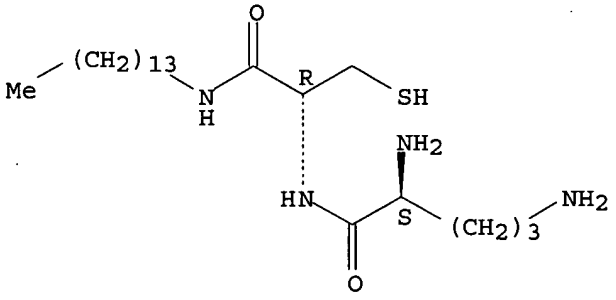
IT **227176-25-2**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(C14-CO; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)
RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L57 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:390393 HCAPLUS
DN 131:40529
ED Entered STN: 24 Jun 1999
TI In situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells
IN Behr, Jean-Paul; Blessing, Thomas; Wagner, Ernst; Schuller, Susanne
PA Boehringer Ingelheim International GmbH, Germany; Universite Louis Pasteur de Strasbourg
SO PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-48
CC 3-1 (Biochemical Genetics)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9929349	A1	19990617	WO 1998-EP7695	19981128
	W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 945138	A1	19990929	EP 1997-121308	19971204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

CA 2312890	AA	19990617	CA 1998-2312890	19981128	
AU 9917577	A1	19990628	AU 1999-17577	19981128	
EP 1037668	A1	20000927	EP 1998-962400	19981128	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

BR 9814255	A	20001010	BR 1998-14255	19981128
JP 2001525378	T2	20011211	JP 2000-524018	19981128
TR 200001597	T2	20020321	TR 2000-20000159719981128	
EE 200000797	A	20020617	EE 2000-20000079719981128	
ZA 9811011	A	19990604	ZA 1998-11011	19981202
NO 2000002793	A	20000801	NO 2000-2793	20000531
PRAI EP 1997-121308	A	19971204		
WO 1998-EP7695	W	19981128		

OS MARPAT 131:40529

AB A method of generating particulate charge-balanced complexes of nucleic acids and cationic polymers by complexing cationic polymers with the DNA and then polymerizing them in situ on the DNA template is described. Discrete, stable particles are obtained by complexing the nucleic acid mols. with identical or different organic cationic precursor without crosslinking the nucleic acid mols., and covalently linking the precursor mols. to each other on the nucleic acid template. For specific cellular targeting, the particles may carry targeting mols., e.g. sugars. Preferred cationic precursor mols. are lipophilic detergents that are linked to form lipids. The particles contain preferably only one nucleic acid mol. which makes them useful for gene therapy and for delivery of large DNA mols. Guanidinylcysteine decylamide was prepared by Boc chemical The detergent oxidized rapidly in air in the presence of DNA to give a uniform population of spheres of 23 nm diameter Transformation of BNL CL.2 cells with a luciferase reporter plasmid incorporated into these complexes is described. Efficiency of transformation was comparable to that of polyethyleneimine as counterion. Synthesis and characterization of other polymerizable cationic detergents is described.

ST cationic detergent polymn DNA template transformation; transformation DNA cationic detergent polymer

IT Adenoviridae
(as endosomolytic agent in transformation using cationic detergent polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Polyelectrolytes
(cationic, formation in situ of; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Detergents
(cationic, polymerization on DNA templates of; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(endosomolytic, in transformation using cationic detergent polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Gene therapy
Transformation, genetic
(in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Critical micelle concentration

(of lipophilic cysteine esters, effects of DNA on; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, derivs., polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT 227176-22-9DP, polymeric oxidation products 227176-23-0DP, polymeric oxidation products **227176-24-1DP**, polymeric oxidation products **227176-25-2DP**, polymeric oxidation products
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in preparation cationic polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT 107-13-1, 2-Propenenitrile, reactions 110-60-1, 1,4-Butanediamine 121-44-8, reactions 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 7087-68-5, N,N-Diisopropylethylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation cationic polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT 52-90-4DP, L-Cysteine, esters with long chain alcs., reactions 31202-58-1DP, N,S-Bis-tert-butoxycarbonyl-L-cysteine, esters with long chain alcs. 31202-58-1P, N,S-Bis-tert-butoxycarbonyl-L-cysteine 33643-55-9P 152120-54-2P 152120-61-1P 177213-61-5P 194808-59-8P 213468-19-0P 213468-20-3P 227176-07-0P 227176-08-1P 227176-09-2P 227176-11-6P 227176-12-7P 227176-13-8P 227176-14-9P 227176-16-1P 227176-17-2P 227176-18-3P 227176-19-4P 227176-20-7P 227176-21-8P 227176-26-3P 227176-27-4P 227176-28-5DP, polymeric oxidation products 227176-31-0P 227176-32-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation cationic polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT 227176-10-5DP, polymeric oxidation products
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

IT 71-44-3DP, Spermine, derivs., polymers 15939-25-0DP, polymeric oxidation products 68643-21-0DP, polymeric oxidation products 100678-92-0DP, polymeric oxidation products 227176-15-0DP, polymeric oxidation products
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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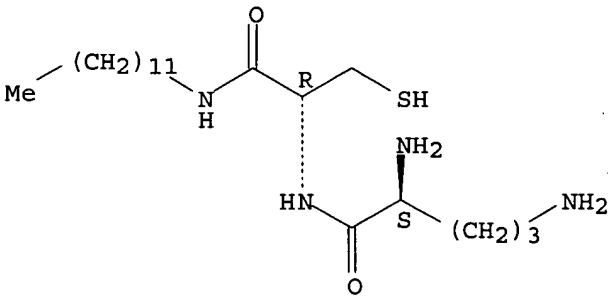
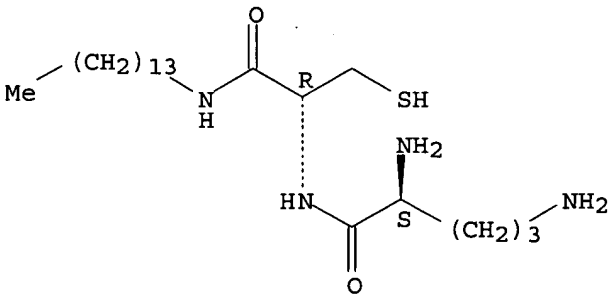
IT [redacted]**227176-24-1DP**, polymeric oxidation products **227176-25-2DP**, polymeric oxidation products
L: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in preparation cationic polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)
RN 227176-24-1 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-dodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 227176-25-2 HCAPLUS
CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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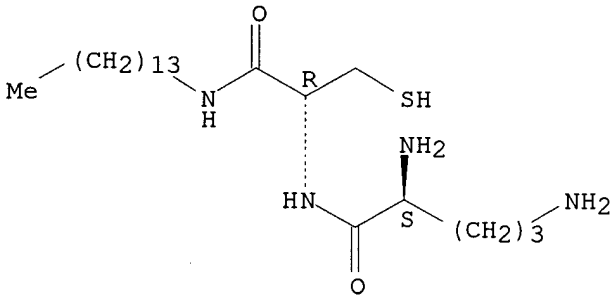
L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS

IT **227176-25-2DP**, complexes with DNA
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intracellular delivery of nanometric DNA particles via the folate receptor)

RN 227176-25-2 CAPLUS

CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 2002:457871 CAPLUS
DOCUMENT NUMBER: 137:174731
TITLE: Intracellular Delivery of Nanometric DNA Particles via the Folate Receptor
AUTHOR(S): Dauty, Emmanuel; Remy, Jean-Serge; Zuber, Guy; Behr, Jean-Paul
CORPORATE SOURCE: Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de Strasbourg Faculte de Pharmacie BP 24, CNRS/Universite Louis Pasteur de Strasbourg, Illkirch, 67401, Fr.
SOURCE: Bioconjugate Chemistry (2002), 13(4), 831-839
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The size of condensed DNA particles is a key determinant for both diffusion to target cells in vivo and intracellular trafficking. The smallest complexes are obtained when each DNA mol. collapses individually. This was achieved using a designed cationic thiol-detergent, tetradecyl-cysteinyl-ornithine (C14COrn). The resulting particles were subsequently stabilized by air-induced dimerization of the detergent into a disulfide lipid on the DNA template. Particles are anionic (zeta potential = -45 mV), and their size (30 nm) corresponds to the vol. of a single plasmid DNA mol. The electrophoretic mobility of the condensed DNA, though quasi-neutralized, was found higher than that of the extended DNA. Moreover, the dimerized (C14COrn)2 lipid was found to be an efficient transfection reagent for various cell lines. In an attempt to achieve extended circulation times and to target tumors by systemic delivery, we have coated the particles with PEG-folate residues. Plasmid DNA was condensed into monomol. particles as described above and coated by simple mixing with DPPE-PEG-folate. Physicochem. measurements showed particles coated with 2% of DPPE-PEG3400-folate remain monomol. and are stable in the cell-culture medium. Caveolae-mediated cell entry was demonstrated by ligand-dependence, by competition with excess folic acid as well as by confocal microscopy.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

IT **227176-25-2P**

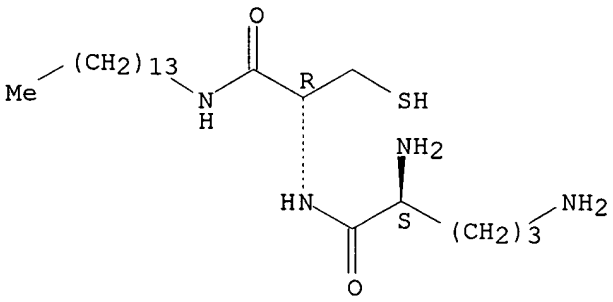
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(thiol cationic detergent; dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture)

RN 227176-25-2 CAPLUS

CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 2001:636468 CAPLUS

DOCUMENT NUMBER: 135:252520

TITLE: Dimerizable Cationic Detergents with a Low cmc Condense Plasmid DNA into Nanometric Particles and Transfect Cells in Culture

AUTHOR(S): Dauty, Emmanuel; Remy, Jean-Serge; Blessing, Thomas; Behr, Jean-Paul

CORPORATE SOURCE: Laboratoire de Chimie Genetique, CNRS/Universite Louis Pasteur de Strasbourg Faculte de Pharmacie, Illkirch, 67401, Fr.

SOURCE: Journal of the American Chemical Society (2001), 123(38), 9227-9234
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The size of condensed DNA particles is a key determinant for in vivo diffusion and gene delivery to cells. Gene mols. can be individually compacted by cationic thiol detergents into nanometric particles that are stabilized by oxidative conversion of the detergent into a gemini lipid. To reach the other goal, gene delivery, a series of cationic thiol detergents with various chain lengths (C12-C16) and headgroups (ornithine or spermine) was prepd., using a versatile polymer-supported synthetic strategy. Crit. micelle concns. and thiol oxidn. rates of the detergents were measured. The formation and stability of complexes formed with plasmid DNA, as well as the size, .xi.-potential, morphol., and transfection efficiency of the particles were investigated. Using the tetradecane/ornithine detergent, a soln. of 5.5 Kpb plasmid DNA mols. was converted into a homogeneous population of 35 nm particles. The same detergent, once oxidized, exhibited a typical lipid phase internal structure and was capable of effective cell transfection. The particle size did not increase with time. Surprisingly, the gel electrophoretic mobility of the DNA complexes was found to be higher than that of plasmid DNA itself. Favorable in vivo diffusion and intracellular trafficking properties may thus be expected for these complexes.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

IT **227176-25-2**

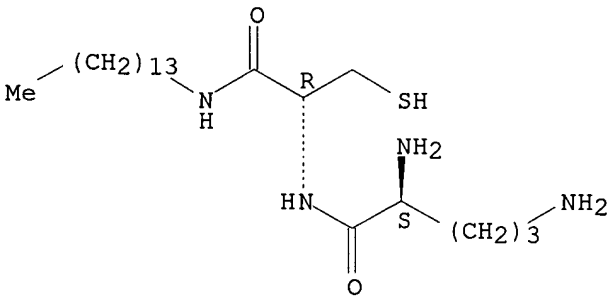
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)

(C14-CO; DNA condensation by an oxidizable cationic detergent and interactions of DNA/detergent complexes with lipid vesicles)

RN 227176-25-2 CAPLUS

CN L-Cysteinamide, L-ornithyl-N-tetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 2001:483530 CAPLUS

DOCUMENT NUMBER: 136:195946

TITLE: DNA condensation by an oxidizable cationic detergent. Interactions with lipid vesicles

AUTHOR(S): Lleres, D.; Dauty, E.; Behr, J.-P.; Mely, Y.; Duportail, G.

CORPORATE SOURCE: UMR 7034 du CNRS, Laboratoire de Pharmacologie et Physicochimie des Interactions Cellulaires et Moleculaires, Illkirch, 67401, Fr.

SOURCE: Chemistry and Physics of Lipids (2001), 111(1), 59-71
CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

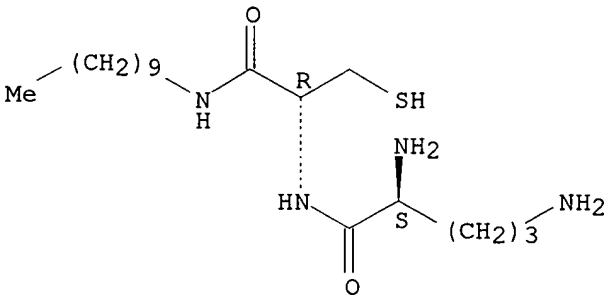
AB Cationic amphiphile-mediated delivery of plasmid DNA is the non-viral gene transfer method most often used. In the present work, we considered a new cysteine-detergent, ornithinyl-cysteinyl-tetradecylamide (C14-CO), able to convert itself, via oxidative dimerization, into a cationic cystine-lipid. By using fluorescence techniques, we first characterized the structure of complexes of plasmid DNA with C14-CO mols. either kept as monomers, or oxidized into dimers. Both forms are able to condense DNA, with the formation of hydrophobic micelle-like domains along the DNA chain. Domains with a larger mol. order were obtained with dimeric C14-CO/DNA complexes. In a second step, the interactions of these complexes with lipid vesicles considered as membrane models were investigated. In the presence of vesicles, we obsd. a decondensation of the DNA involved in complexes obtained with C14-CO monomers. With anionic vesicles, the DNA is released into the bulk soln., while with neutral vesicles, it remains bound to the vesicles via electrostatic interactions with inserted C14-CO mols. In sharp contrast, the complexes with C14-CO dimers are unaffected by the addn. of either neutral or anionic vesicles and show no interaction with them. These results may partly explain the low transfection efficiency of these complexes at the .+-. charge ratios used in this study.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
IT **227176-23-0DP**, polymeric oxidn. products
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in prepn. cationic polymers; in situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells)
RN 227176-23-0 CAPLUS
CN L-Cysteinamide, L-ornithyl-N-decyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1999:390393 CAPLUS
DOCUMENT NUMBER: 131:40529
TITLE: In situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells
INVENTOR(S): Behr, Jean-Paul; Blessing, Thomas; Wagner, Ernst; Schuller, Susanne
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Universite Louis Pasteur de Strasbourg
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929349	A1	19990617	WO 1998-EP7695	19981128
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 945138	A1	19990929	EP 1997-121308	19971204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2312890	AA	19990617	CA 1998-2312890	19981128
AU 9917577	A1	19990628	AU 1999-17577	19981128
EP 1037668	A1	20000927	EP 1998-962400	19981128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9814255	A	20001010	BR 1998-14255	19981128
JP 2001525378	T2	20011211	JP 2000-524018	19981128
ZA 9811011	A	19990604	ZA 1998-11011	19981202
NO 2000002793	A	20000801	NO 2000-2793	20000531

PRIORITY APPLN. INFO.: EP 1997-121308 A 19971204
WO 1998-EP7695 W 19981128

OTHER SOURCE(S): MARPAT 131:40529

AB A method of generating particulate charge-balanced complexes of nucleic acids and cationic polymers by complexing cationic polymers with the DNA and then polymg. them in situ on the DNA template is described. Discrete, stable particles are obtained by complexing the nucleic acid mols. with identical or different org. cationic precursor without crosslinking the nucleic acid mols., and covalently linking the precursor mols. to each other on the nucleic acid template. For specific cellular targeting, the particles may carry targeting mols., e.g. sugars. Preferred cationic precursor mols. are lipophilic detergents that are linked to form lipids. The particles contain preferably only one nucleic acid mol. which makes them useful for gene therapy and for delivery of large DNA mols. Guanidinylcysteine decylamide was prepd. by Boc chem. The detergent oxidized rapidly in air in the presence of DNA to give a uniform population of spheres of 23 nm diam. Transformation of BNL CL.2 cells with a luciferase reporter plasmid incorporated into these complexes is described. Efficiency of transformation was comparable to that of polyethyleneimine as counterion. Synthesis and characterization of other polymerizable cationic detergents is described.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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nucleic acid mols., and covalently linking the precursor mols. to each other on the nucleic acid template. For specific cellular targeting, the particles may carry targeting mols., e.g. sugars. Preferred cationic precursor mols. are lipophilic detergents that are linked to form lipids. The particles contain preferably only one nucleic acid mol. which makes them useful for gene therapy and for delivery of large DNA mols. Guanidinylcysteine decylamide was prepd. by Boc chem. The detergent oxidized rapidly in air in the presence of DNA to give a uniform population of spheres of 23 nm diam. Transformation of BNL CL.2 cells with a luciferase reporter plasmid incorporated into these complexes is described. Efficiency of transformation was comparable to that of polyethyleneimine as counterion. Synthesis and characterization of other polymerizable cationic detergents is described.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

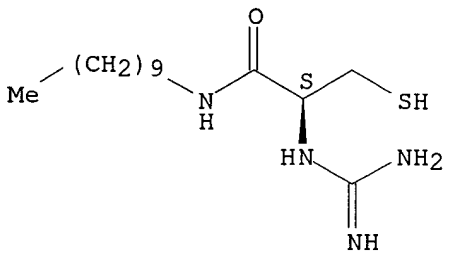
L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

IT **213468-23-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(template oligomerization of DNA-bound cations produces calibrated nano-metric particles)

RN 213468-23-6 CAPLUS

CN Propanamide, 2-[(aminoiminomethyl)amino]-N-decyl-3-mercapto-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1998:499492 CAPLUS
DOCUMENT NUMBER: 129:260731
TITLE: Template Oligomerization of DNA-Bound Cations Produces Calibrated Nanometric Particles
AUTHOR(S): Blessing, Thomas; Remy, Jean-Serge; Behr, Jean-Paul
CORPORATE SOURCE: Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de Strasbourg (UMR 7514) Faculte de Pharmacie, Illkirch, 67401, Fr.
SOURCE: Journal of the American Chemical Society (1998), 120(33), 8519-8520
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

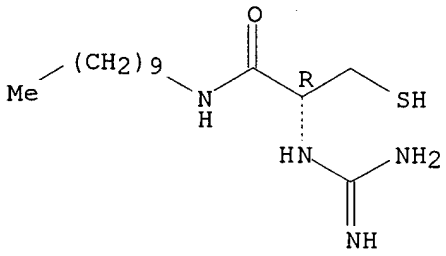
AB A general approach to the monomol. condensation of DNA into stable nano-metric particles is reported, which may be extended to the design of any kind of calibrated nano-metric particles required for material sciences. The process takes advantage of the low cooperativity of binding small monomeric counterions to a macromol. polyion, followed by a zipper-oligomerization reaction which "freezes" the resulting condensed particles. The DNA particles have a neg. surface charge which ensures colloid stability and in vivo diffusion, yet makes them unsuitable for carrying DNA into cells. Thus, C-sper-C [cysteine-spermine-cysteine (I)] was synthesized and mixed with plasmid DNA, which was found to enhance the

thiol oxidn. rates in the thiol/disulfide oligomerization, which resulted in condensation of the DNA into particles of mean size 50 .+-. 15 nm, which were stable .gtoreq.1 wk. The condensed particles were stable in electrophoresis conditions, but addn. of excess dithiothreitol of raising the ionic concn. to physiol. levels converted the cationic polymer back to I.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

acids for delivery to animal cells)
RN 227176-10-5 CAPLUS
CN Propanamide, 2-[(aminoiminomethyl)amino]-N-decyl-3-mercapto-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



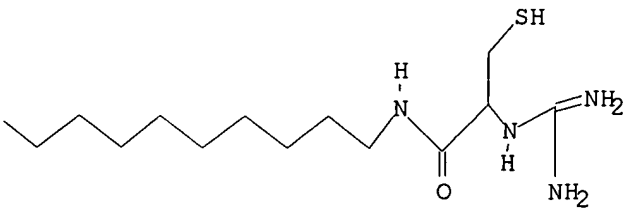
ACCESSION NUMBER: 1999:390393 CAPLUS
DOCUMENT NUMBER: 131:40529
TITLE: In situ formation of particulate complexes of polycations and nucleic acids for delivery to animal cells
INVENTOR(S): Behr, Jean-Paul; Blessing, Thomas; Wagner, Ernst; Schuller, Susanne
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Universite Louis Pasteur de Strasbourg
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929349	A1	19990617	WO 1998-EP7695	19981128
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 945138	A1	19990929	EP 1997-121308	19971204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2312890	AA	19990617	CA 1998-2312890	19981128
AU 9917577	A1	19990628	AU 1999-17577	19981128
EP 1037668	A1	20000927	EP 1998-962400	19981128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9814255	A	20001010	BR 1998-14255	19981128
JP 2001525378	T2	20011211	JP 2000-524018	19981128
ZA 9811011	A	19990604	ZA 1998-11011	19981202
NO 2000002793	A	20000801	NO 2000-2793	20000531

PRIORITY APPLN. INFO.: EP 1997-121308 A 19971204
WO 1998-EP7695 W 19981128
OTHER SOURCE(S): MARPAT 131:40529

AB A method of generating particulate charge-balanced complexes of nucleic acids and cationic polymers by complexing cationic polymers with the DNA and then polymg. them in situ on the DNA template is described. Discrete, stable particles are obtained by complexing the nucleic acid mols. with identical or different org. cationic precursor without crosslinking the

L8 STR



Structure attributes must be viewed using STN Express query preparation.
L9 2 SEA FILE=REGISTRY SSS FUL L8
L10 3 SEA FILE=CAPLUS ABB=ON PLU=ON L9

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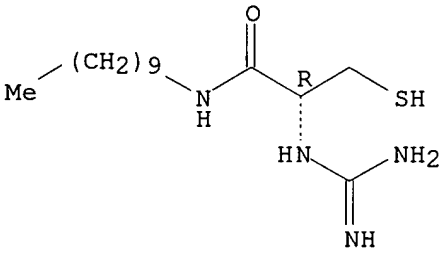
L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
IT **227176-10-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dimerizable detergents as gene transfer vectors)
RN 227176-10-5 CAPLUS
CN Propanamide, 2-[(aminoiminomethyl)amino]-N-decyl-3-mercapto-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 2001:52575 CAPLUS
DOCUMENT NUMBER: 135:277883
TITLE: Dimerizable detergents as gene transfer vectors
AUTHOR(S): Blessing, Thomas; Dauty, Emmanuel; Remy, Jean-Serge; Behr, Jean-Paul
CORPORATE SOURCE: Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur, Faculte de Pharmacie de Strasbourg, Illkirch, 67401, Fr.
SOURCE: Journal of Liposome Research (2000), 10(4), 321-327
CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cationic lipids are efficient vectors for DNA delivery in vitro. However, they condense DNA into large polymorphic particles, which severely limits their in vivo performances due to size-restricted diffusion. In contrast, detergents are capable of collapsing DNA into smaller particles but do not mediate cell transfection per se. We have succeeded in retaining the interesting features of both types of amphiphiles in a two-step process leading to monomol. DNA particles stable in physiol. medium. Anionic DNA mols. were first individually condensed with a designed cationic cysteine-based detergent. The resulting small particles were then stabilized by spontaneous thiol dimerization of the cysteine-detergent into a cystine-lipid on the template DNA. Laser light scattering as well as electron microscopy revealed a monodisperse population of spherical particles that were stable for days in physiol. conditions. With an appropriate choice of hydrocarbon chain length, monomol. complexes exhibiting a typical lipid/DNA internal structure could be obtained. Their in vitro cell transfection properties compare favorably with those of Lipofectamine and PEI.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
IT **227176-10-5DP**, polymeric oxidn. products
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(in situ formation of particulate complexes of polycations and nucleic

Palmitoyl derivatives of L-**cysteine** , cysteamine, L-cystine, cystamine and their incorporation into the bilayers of unilamellar **liposomes**.

Schott H; Seeling R; Hengartner H; Schwendener RA
Institut fur Organische Chemie, Universitat Tubingen, F.R.G.

Biochimica et biophysica acta (NETHERLANDS) May 9 **1988**, 940 (1) p127-35, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The amino groups of the amino acids L-**cysteine** and L-cystine as well as their biogene amines cysteamine and cystamine were derivatized with palmitoyl residues. The obtained lipophilic R-**SH** and R-S-S-R components were incorporated into the bilayers of unilamellar **liposomes**. The resulting **liposomes** carrying about 2000 functional groups each remained stable and homogeneous during 60 days after incorporation of N-palmitoyl cysteamine and N,N'-dipalmitoyl cystamine. The incorporation of the lipophilic amino acid derivatives, however, destabilized the resulting **liposomes**. Via the thiol residues of the functionalized **liposomes** activated molecules can be linked to the **liposomal** surface by disulfide bonds

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Set     Items   Description
S1       3220   CYSTEIN? AND ALKYL?
S2          6   S1 AND (VESIC? OR LIPOSOM?) AND DNA
S3          4   RD (unique items)
S4          1   ALKYLENE (W) SH
? s s1 and sh

            3220  S1
           22926  SH
      S5     203  S1 AND SH
? rd

...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...completed examining records
      S6     155  RD (unique items)
? s s6 and py<1998

Processing
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        20863023  PY<1998
      S7     131  S6 AND PY<1998
? s s7 and dna

             131  S7
         1258748  DNA
      S8      11  S7 AND DNA
? t s8/3,ab/all


 8/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08487942   95221436   PMID: 7706318
   beta-Cystathionase from Bordetella avium. Role(s) of lysine 214 and
cysteine residues in activity and cytotoxicity.
  Gentry-Weeks CR; Spokes J; Thompson J
  Laboratory of Microbial Ecology, NIDR, National Institutes of Health,
Bethesda, Maryland 20892, USA.
  Journal of biological chemistry (UNITED STATES)   Mar 31 1995,  270
  (13)  p7695-702,  ISSN 0021-9258   Journal Code: HIV
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  beta-Cystathionase (EC 4.4.1.8) from Bordetella avium is a pyridoxal
5'-phosphate (PLP)-dependent enzyme that catalyzes the hydrolysis of
L-cystine to yield pyruvic acid, NH3, and thiocysteine. The latter compound
is highly toxic toward MC3T3-E1 osteogenic cells, rat osteosarcoma cells,
and other cell lines maintained in tissue culture (Gentry-Weeks, C. R.,
Keith, J. M., and Thompson, J. (1993) J. Biol. Chem. 268, 7298-7314).
Site-directed mutagenesis has established that lysine 214 of the sequence
TKYVGGHSD, is primarily responsible for internal aldimine binding of PLP in
the holoenzyme. Translation of the DNA sequence of the
beta-cystathionase gene (metC) from B. avium, reveals 4 cysteine
residues/enzyme subunit (M(r) = 42,600), and spectrophotometric analysis
with 4,4'-dithiodipyridine showed that there were no disulfide linkages in
the native protein. beta-Cystathionase is inhibited by sulfhydryl-reactive
agents, including N-ethylmaleimide (NEM). To elucidate the mechanism of NEM
inhibition, each of the 4 cysteine residues at positions 88, 117,
279, and 309 was individually replaced by alanine or glycine. The mutant
proteins C88A, C117G, C279G, and C309A were purified to homogeneity, and
each was assayed for enzyme activity, PLP-binding, NEM sensitivity, and
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susceptibility to chymotrypsin digestion. The activities of mutant proteins C88A and C279G were comparable with that of the native enzyme, and since both forms were inhibited by NEM, neither **cysteine** 88 nor 279 are prerequisite for enzyme activity. By elimination, **cysteine** residues 117 and 309 must be the targets for **alkylation**, and resultant inactivation of beta-cystathionase, by the -**SH** reactive agent. Substitution of **cysteine** 117 and 309 with glycine and alanine, respectively, yielded the inactive proteins C117G and C309A. PLP was not detectable in these proteins, and their absorption spectra lacked the peak (at 420 nm) that is characteristic of internal PLP-Schiff base formation. Edman degradation revealed that C117G (M(r) approximately 36,000) also lacked the first 63 amino acids comprising the N terminus of the native protein. The beta-cystathionase mutants C117G and C309A showed enhanced susceptibility to chymotrypsin digestion. **Cysteine** residues 117 and 309 may reside in conformationally sensitive environments, and in the native enzyme these amino acids most probably serve a structural function. Toxicity assays performed with the various mutant proteins obtained by site-directed mutagenesis established that only catalytically active forms of beta-cystathionase were were cytotoxic for tissue culture cells.

8/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07854766 93185605 PMID: 8444143
Effects of methyl methanesulfonate on mouse sperm chromatin structure and testicular cell kinetics.
Evenson DP; Jost LK; Baer RK
Olson Biochemistry Laboratory, Department of Chemistry, South Dakota State University, Brookings 57007.
Environmental and molecular mutagenesis (UNITED STATES) **1993**, 21 (2) p144-53, ISSN 0893-6692 Journal Code: EMM
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Effects of methyl methanesulfonate (MMS) on mouse testicular cell kinetics and sperm chromatin structure were determined flow cytometrically. Mice were exposed to a single ip injection of saline containing 0 or 150 mg/kg MMS. Relative ratios of 1N, 2N and 4N testicular cells were not affected until 22 days postexposure. Ratios of 1N cell types were altered from 13 to 22 days and were near normal by 25 days. This study revealed an MMS induced alteration of chromatin structure in testicular, elongated spermatids by the sperm chromatin structure assay (SCSA), a flow cytometric measure of the susceptibility of acridine orange stained sperm **DNA** to denaturation in situ. The SCSA also detected alterations in cauda sperm chromatin structure at 3 days, which was 8 days prior to alterations in sperm head morphology, indicating the increased sensitivity of the SCSA. SCSA data were practically similar whether measuring either fresh or frozen/thawed sperm, or whether measured by two different types of flow cytometers: a) laser driven, orthogonal optical axis; or b) low cost mercury arc lamp system with epiillumination. The data support the model of Sega and Owens [Mutat Res 111:227-244:1983] that MMS **alkylates cysteine-SH** groups in sperm protamines, thereby destabilizing sperm chromatin structure and leading to broken chromosomes and mutations.

8/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07527385 91254152 PMID: 1645950
Cadmium/zinc-metallothionein induces **DNA** strand breaks in vitro.
Muller T; Schuckelt R; Jaenicke L
INBIFO Institut fur biologische Forschung, Koln, Federal Republic of Germany.

Archives of toxicology (GERMANY) **1991**, 65 (1) p20-6, ISSN 0340-5761 Journal Code: 8J7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The in vitro **DNA** strand breaking activity of metallothionein (MT) containing Cd2+ and Zn2+ in a molar ratio of 5:2 is described. Studies with radical scavengers and electron paramagnetic resonance spectroscopy indicate that the **DNA** damage might be caused by a radical species formed by the native protein (i.e., MT) charged with the heavy metal ions. No **DNA** strand breaks are detectable with the heat-denatured MT or with Cd2+ or Zn2+ alone. Inhibition studies using EDTA as a metal ion chelator or N-ethylmaleimide to **alkylate** sulfhydryl groups suggest that both the bound heavy metal ions as well as the **SH** groups of the various **cysteine** residues of MT may be involved in the MT-dependent **DNA** cleavage. Further characterization showed that the **DNA** cleavage is more likely random than sequence- or base-specific. These observations may provide a clue in the search for initial events in Cd-related carcinogenicity.

8/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07164388 91183540 PMID: 2009579
Dealkylation rates of O6-**alkyldeoxyguanosine**, O4-**alkylthymidine** and related compounds in an **alkyl**-transfer system.
Kohda K; Yasuda M; Sawada N; Itano K; Kawazoe Y
Faculty of Pharmaceutical Sciences, Nagoya City University, Japan.
Chemico-biological interactions (NETHERLANDS) **1991**, 78 (1) p23-32, ISSN 0009-2797 Journal Code: CYV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Bacterial O6-**alkylguanine-DNA alkyltransferase** (AGT) removes **alkyl** group from O6-**alkylguanine** and O4-**alkylthymine** residues in **DNA**, both of which are considered to be **DNA** damages most related to the induction of cancer and/or mutation. The repair process involves **alkyl**-transfer of an O-**alkyl** group to the active site of the enzyme, where an **SH**-group of **cysteine** residue plays the role of **alkyl** acceptor. In order to elucidate the chemical characteristics of substrates for this enzyme, dealkylation rates of O6-**alkyldeoxyguanosine**, O4-**alkylthymidine** and related compounds were measured using an **alkyl**-transfer system. Thiophenol-triethylamine system was employed as an **alkyl** acceptor and twenty-one O-**alkyl** compounds were tested. Dealkylation proceeded with pseudo first order kinetics. The half-life of O6-methyldeoxyguanosine (MedG) was 122 h and no remarkable dependence on N-9 substituents (H, CH3 and deoxyribose) was observed. A compound lacking 2-NH2 group underwent demethylation about three times faster than O6-methylguanines did, while, a compound lacking imidazole moiety underwent demethylation about 2.5 times more slowly. The half-life of O4-methylthymidine (MedT) was 38 h and no remarkable dependence on N-1 (H, CH3 and deoxyribose) and C-5 (H and CH3) substituents was observed. Deethylation proceeded much more slowly than demethylation. Substitution of selenophenol for thiophenol resulted in a 4.5 times faster MedG demethylation rate. Demethylation rates were moderately correlated with values for NMR chemical shift of CH3 group, an indicator of electron density, although the correlation curves of a series of MedG and MedT derivatives were quite different. This result suggests that some different rate-determining factors other than electron density are playing a role. These findings may be of help in resolving the details of the mechanisms of enzymic repair by bacterial and mammalian AGT.

8/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05983879 85225755 PMID: 2408626
The role of sulfhydryl groups in the functioning of **DNA**-dependent RNA-polymerase]
Rol' sul'fgidril'nykh grupp v funktsionirovanii DNK-zavisimoi RNK-polimerazy.
Chertov OIu; Seliuchenko OA; Lipkin VM
Bioorganicheskaia khimiia (USSR) Apr **1985**, 11 (4) p492-8,
ISSN 0132-3423 Journal Code: 9Z8
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
Sulfhydryl groups of Escherichia coli **DNA**-dependent RNA polymerase were chemically modified with **alkylating** and mercuric-containing compounds. Iodoacetic acid and iodoacetamide were shown not to affect the enzymatic activity, whereas N-ethylmaleimide and mercuric-containing compounds completely inhibit the RNA synthesis. RNA polymerase modified with mercuric ions looses the ability of binding with promoter--containing **DNA** fragments. Moreover, mercuric ions inhibit the RNA elongation stage. Suggestion is made the Cys residues of RNA polymerase play a key role in double-stranded **DNA** unwinding. It is shown that **SH** -groups of beta- and beta'-subunits participate in the binding with double-stranded fragments of **DNA**.

8/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04603838 85096220 PMID: 6517706
Analysis of hemoglobin as a dose monitor for **alkylating** and arylating agents.
Neumann HG
Archives of toxicology (GERMANY, WEST) Nov **1984**, 56 (1) p1-6,
ISSN 0340-5761 Journal Code: 8J7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Genotoxic xenobiotics bind covalently to hemoglobin in vivo. The major reaction product of aromatic amines is a sulfinic acid amide resulting from the reaction of arylnitroso derivatives with **SH**-groups. **Alkylating** compounds react with **cysteine**, histidine and the terminal valine. The adducts are formed proportional to dose down to extremely small doses, they are stable throughout the life-span of the erythrocytes and accumulate upon repeated exposure. Methods for their determination in blood samples from experimental animals and humans are becoming available. Moreover, it has been demonstrated that for a given agent, a constant ratio exists between the reaction with tissue **DNA** and hemoglobin over a wide range of doses, which indicates that the reactions follow apparent first order kinetics. The extent of hemoglobin binding is therefore considered to be a relative measure of tissue dose, and should correlate much better with risk than exposure levels calculated from concentrations in the environment. Not only can the actual uptake be monitored more reliably, but also the individual's capacity to metabolically activate the absorbed agent. Biomonitoring of hemoglobin-bound metabolites represents a novel approach to control exposure to potential carcinogens, to correlate environmental exposure with tissue dose and eventually also with human risk.

8/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02439278 77143880 PMID: 845864
Antitumor agents. 21. A proposed mechanism for inhibition of cancer growth by tenulin and helenalin and related cyclopentenones.
Hall IH; Lee KH; Mar EC; Starnes CO; Waddell TG
Journal of medicinal chemistry (UNITED STATES) Mar **1977**, 20 (3) p333-7, ISSN 0022-2623 Journal Code: J0F
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Evidence is presented that sesquiterpene lactones or ketones containing the O=CC=CH2 moiety, e.g., tenulin and helenalin, **alkylate** the thiol group of reduced glutathione and L-**cysteine** in vitro. A proposal is offered that this mechanism of action is responsible for the observed potent in vivo antitumor activity of these agents in the Ehrlich ascites and Walker 256 carcinosarcoma and to a lesser extent in the P388 leukemic screen. Inhibition of tumor growth is thought to occur due to the O=CC=CH2 system **alkylating** by rapid Michael addition the **SH** biological nucleophiles of key regulatory enzymes of nucleic acid and chromatin metabolism. This proposition is in accord with the ability of these agents to inhibit **DNA** synthesis and gene activity of Ehrlich ascites cells.

8/3,AB/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09173982 BIOSIS NO.: 199497182352
The subtlety of **alkylating** agents in reactions with biological macromolecules.
AUTHOR: Vogel Ekkehart W(a); Nivard Madeleine J M
AUTHOR ADDRESS: (a)Med. Genetics Centre South-West Neth., MGC, Dep. Radiation Genetics Chemical Mutagenesis, Sylviu**Netherlands
JOURNAL: Mutation Research 305 (1):p13-32 **1994**
ISSN: 0027-5107
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Genotoxic agents known to modify **DNA** by **alkylation** reactions (**alkylating** agents, AAs), either directly or after metabolic conversion to ultimately reactive intermediates, by no means represent a homogeneous class. For instance, their effectiveness for genotoxic damage, when expressed as the number of events (e.g., mutations) per unit exposure dose, varies over a more than 1-million-fold range in dose. Despite the multiplicity of chemical and biological processes involved between **DNA** adduct formation and expression of genotoxic damage, the principal aims of studies on structure-activity relationships (SARs) are to (a) dissect the multi-step process of genetic damage formation into its most essential components, (b) use SARs for making predictions and, at a later step (c) as a basis for regulatory measures. The analytical tools available for such a comprehensive analysis in eukaryotic systems include determination of multiple genetic endpoints: molecular mutation spectra, relative clastogenicity (clastogenic events in relation to forward mutation induction) and the quantitative measure of enhanced mutagenicity in repair-deficient conditions. The genetic activity profiles obtained in this way can then be compared with fundamental physico-chemical properties of the AAs under consideration (such as Swain-Scott's s value, a useful indicator of the selectivity of an AA in its reactions with nucleophiles of distinct nucleophilic strength n in **DNA**, RNA and proteins), their functionality (monofunctional versus cross-linking) and their tumorigenic potency (TD-50s compared with measures of initial **DNA** interaction, i.e., O-6-/N7-**alkylguanine** ratios, s values or the covalent binding

index determined in the liver in vivo). The combination of these different methods revealed that carcinogenic potencies of AAs in rodents vary over a 10,000-fold range in dose, with the extremes having the following characteristics: (i) Chemicals of a relatively "high carcinogenic potency", as indicated by a low TD-50 in rodents, either have low nucleophilic selectivity (and therefore mainly act through O-**alkylation** in **DNA**) or are capable of cross-linking **DNA**. The monofunctional members of the group, typified by N-ethyl-N-nitrosourea, are active in both spermatogonia and post-spermatogonial stages in the mouse and in Drosophila. Cross-linking agents also have a low TD-50 value in rodents but are expected generally not to display genetic action in premeiotic stages (exceptions mitomycin C and chlorambucil). (ii) A relatively low carcinogenic potential is associated with AAs of high Swain-Scott s values, typified by trimethyl phosphate, epichlorohydrin or methyl methanesulphonate. Efficient error-free repair of N-**alkylation** damage appears the responsible mechanism for their high TD-50 in rodents and why they tend to be inactive in repair-competent germ cells of the mouse. Since AAs of high s values give relatively high degrees of **alkylation** of proteins (e.g., with the -**SH** group of esterified **cysteine**, n = 5.1) reaction products with strong nucleophiles are often formed in amounts orders of magnitude larger than the products at n = 2 (**DNA**). As a consequence, the "window" of the dose range not causing cell lethality but, at the same time, still producing a significant amount of damage (e.g., mutations) will be very small. These type of agents are expected to be "trouble-makers" particularly in the in vivo mutagenicity assays. Examples are acrolein, chloroethyl isocyanate, chloroethylene oxide (s = 0.71), epichlorohydrin (s = 0.93), 1,2-epoxybutane, methyl bromide (s = 1.0), methyl iodide (s = 1.20), methyl vinylsulphone and 2-oxopropyl methanesulphonate (s = 2).

1994

8/3,AB/9 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07639251 BIOSIS NO.: 000092009195
DEALKYLATION RATES OF O-6 **ALKYLDEOXYGUANOSINE** O-4 ALKYLTHYMIDINE AND RELATED COMPOUND IN AN **ALKYL** TRANSFER SYSTEM
AUTHOR: KOHDA K; YASUDA M; SAWADA N; ITANO K; KAWAZOE Y
AUTHOR ADDRESS: FACULTY PHARMACEUTICAL SCIENCE, NAGOYA CITY UNIV., TANABEDORI, MIZUHO-KU, NAGOYA 467, JAPAN.
JOURNAL: CHEM-BIOL INTERACT 78 (1). 1991. 22-32. **1991**
FULL JOURNAL NAME: Chemico-Biological Interactions
CODEN: CBINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Bacterial O6-**alkylguanine-DNA** alkyltransferase (AGT) removes **alkyl** group from O66-**alkylguanine** and O4-alkylthymine residues in **DNA**, both of which are considered to be **DNA** damages most related to the induction of cancer and/or mutation. The repair process involves **alkyl**-transfer of an O-**alkyl** group to the active site of the enzyme, where an **SH**-group of **cysteine** residue plays the role of **alkyl** acceptor. In order to elucidate the chemical characteristics of substrates for this enzyme, dealkyation rates of O6-**alkyldeoxyguanosine**, O4-alkylthymidine and related compounds were measured using an alklyl-transfer system. Thiophenol-triethylamine system was employed as an **alkyl** acceptor and twenty-one O-**alkyl** compounds were tested. Dealkylation proceeded with pseudo first order kinetics. The half-life of O6-methyldeoxyguanosine (MedG) was 122 h and no remarkable dependence on N-9 substituents (H, CH3 and

deoxyribose) was observed. A compound lacking 2-NH2 group underwent demethylation about three times faster than O6-methylguanines did, while, a compound lacking imidazole moiety underwent demethylation about 2.5 times more slowly. The half-life of O4-methylthymidine (MedT) was 38 h and no remarkable dependence on N-1 (H, CH3 and deoxyribose) and C-5 (H and CH3) substituents was observed. Deethylation proceeded much more slowly than demethylation. Substitution of selenophenol for thiophenol resulted in a 4.5 times faster MedG demethylation rate. Demethylation rates were moderately correlated with values for NMR chemical shift of CH3 group, an indicator of electron density, although the correlation curves of a series of MedG and MedT derivatives were quite different. This result suggests that some different rate-determining factors other than electron density are playing a role. These findings may be of help in resolving the details of the mechanisms of enzymic repair by bacterial and mammalian AGT.

1991

8/3,AB/10 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04353743 BIOSIS NO.: 000078083287
METHYLATION OF **DNA** AND PROTAMINE BY METHYL METHANESULFONATE IN THE GERM CELLS OF MALE MICE
AUTHOR: SEGA G A; OWENS J G
AUTHOR ADDRESS: BIOLGOY DIV., OAK RIDGE NATL. LAB., OAK RIDGE, TN 37830, USA.
JOURNAL: MUTAT RES 111 (2). 1982. 227-244. **1982**
FULL JOURNAL NAME: Mutation Research
CODEN: MUREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The molecular dosimetry of methyl methanesulfonate (MMS) in the germ cells of male mice was investigated. The mice were injected i.p. with 100 mg/kg of [3H]MMS and methylations per sperm head, per deoxynucleotide and per unit of protamine were then determined over a 3-wk period. The methylations per sperm head paralleled the dominant lethal frequency curve for MMS, reaching a maximum of between 22 and 26 million methylations per vas sperm head 8-11 days after treatment. Methylation of sperm **DNA** was greatest at 4 h (the earliest time point studied) after treatment, with 16.6 methylations/105 deoxynucleotides. **DNA** methylation gradually decreased during the subsequent 3-wk period. The methylation of germ-cell **DNA** did not increase in the stages most sensitive to MMS (late spermatids .fwdarw. early spermatozoa) and was not correlated with the dominant lethal frequency curve for MMS. Methylation of protamine did increase in the germ-cell stages most sensitive to MMS, and showed an excellent correlation with the incidence of dominant lethals produced by MMS in the different germ-cell stages. The pattern of **alkylation** produced by MMS in the developing germ-cell stages of the mouse is similar to that found for EMS [ethyl methanesulfonate]. For equimolar exposures, MMS **alkylates** the germ cells 5-7 times more than does EMS. Hydrolyzed samples of protamine from [3H]MMS-exposed animals were subjected to TLC and amino acid analysis. Both procedures showed that most of the labeled material recovered from the hydrolysates co-chromatographed with authentic standards of S-methyl-L-**cysteine**. The amino acid analyses showed an average of .apprx. 80% of the labeled material eluting with S-methyl-L-**cysteine**. The mechanism of action of both MMS and EMS on the developing germ cells appears to be similar. The occurrence of S-methyl-L-**cysteine** as the major reaction product in sperm protamine after MMS exposure supports the initial model of how dominant

lethals are induced in mouse germ cells by these chemicals: **alkylation** of **cysteine SH** groups contained in mouse-sperm protamine blocks normal disulfide-bond formation, preventing proper chromatin condensation in the sperm nucleus. Subsequent stresses produced in the chromatin structure eventually lead to chromosome breakage, with resultant dominant lethality.

1982

8/3,AB/11 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03219062 BIOSIS NO.: 000071032173
MODE OF RNA SYNTHESIS INHIBITION BY 1 3 4 THIADIAZOLO-3 2-A-PYRIMIDINES
AUTHOR: SUIKO M; TANIGUCHI E; MAEKAWA K; ETO M
AUTHOR ADDRESS: DEP. AGRIC. CHEM., KYUSHU UNIV., FUKUOKA 812, JPN.
JOURNAL: AGRIC BIOL CHEM 44 (8). 1980. 1923-1928. **1980**
FULL JOURNAL NAME: Agricultural and Biological Chemistry
CODEN: ABCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: When **DNA**-dependent RNA polymerase from Ehrlich ascites tumor cells (E-cells) was directly incubated with 2-ethylsulfonyl-7-methyl-5H-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one (TPSO2-2) and dialyzed to remove the chemical, its transcriptive activity was suppressed. The inhibition of enzyme activity was not restored by the addition of substrates. TPSO2-2 **alkylated** alcohols in the presence of amines. An alkylthio derivative which had no repressing effect on E-cell propagation did not react with alcohols. TPSO2-2 showed a high inhibitory effect against **SH** enzyme, such as yeast alcohol dehydrogenase, but was scarcely inhibited by an alkylthio derivative. TPSO2-2 reacted with L-**cysteine**. The reactivity of the 2-position of 1,3,4-thiadiazolo[3,2-a]-pyrimidines is apparently responsible for biological activity, and RNA polymerase is inactivated by the **alkylation** of the **SH** or OH group with PTSO2-2.

1980

ABSTRACT: The merocyanine 540 (MC540)-mediated reduction of nitroxide spin labels in a **liposomal** system was examined using electron spin resonance (ESR) spectroscopy. Spin label reduction was light driven, and occurred in **liposomes** composed of both fully-saturated (dimyristoyl) and mono-unsaturated (1-palmtoyl-2-oleoyl) phosphatidylcholine. Loss of the nitroxide ESR signal was enhanced by the physiological electron donors glutathione, **cysteine**, and NADPH; and was strongly inhibited by the presence of molecular oxygen. Nitroxides reduced in the presence of MC540 alone could be regenerated either by purging the sample with air or by the addition of ferricyanide, indicating that the ESR signal loss was due to reduction to the corresponding hydroxylamines. Only partial regeneration was attained for nitroxides reduced in the presence of glutathione, **cysteine**, or NADPH. Reduction rates for the lipophilic spin labels, 5-, 12-, and 16-doxyl stearic acid, were not influenced by the position of the nitroxide moiety along the **alkyl** chain, however, reduction of spin labels occupying primarily the aqueous phase was much slower. These studies demonstrate that MC540 can initiate oxidation/reduction (Type I) reactions. Such Type I processes may augment the effects of singlet oxygen in MC540-mediated photodynamic therapy.

1991

7/3,AB/4 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06669471 BIOSIS NO.: 000087111648
SYNTHESIS AND AGGREGATION BEHAVIOR OF CHIRAL **CYSTEINE** AMPHIPHILES WITH S TRIAZINE AS CONNECTING UNIT
AUTHOR: STAATZ I; GRANZER U H; BLUME A; ROTH H J
AUTHOR ADDRESS: PHARMAZEUTISCHES INST. DER UNIV. TUEBINGEN, AUF DER MORGENSTELLE 8, D-7400 TUEBINGEN.
JOURNAL: LIEBIGS ANN CHEM 0 (2). 1989. 127-132. **1989**
FULL JOURNAL NAME: Liebigs Annalen der Chemie
CODEN: LACHD
RECORD TYPE: Abstract
LANGUAGE: GERMAN

ABSTRACT: Several homologous **liposome** building blocks 3 with L-**cysteine** as chiral hydrophilic head group are synthesized. s-Triazine serves as connecting unit between **cysteine** and the lipophilic **alkyl** chains. The phase transition temperatures of the lipids are determined by DSC or fluorescence anisotropy. It can be shown, that the relationship between nature and length of the chains and the phase transition temperature corresponds to that of phospholipids. Encapsulation experiments with ionic water-soluble dyes given some hints that the vesicles prepared in phosphate buffer (pH = 7.0) interact with cationic but not with anionic hydrophilic substances.

1989

7/3,AB/5 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06647200 BIOSIS NO.: 000087089377
SYNTHESIS OF CHIRAL **LIPOSOME** BUILDING BLOCKS WITH S TRIAZINE AS LINKING UNIT
AUTHOR: STAATZ I; GRANZER U H; ROTH H J
AUTHOR ADDRESS: PHARMAZEUTISCHES INST. DER UNIVERSITAET TUEBINGEN, AUF DER MORGENSTELLE 8, D-7400 TUEBINGEN.

JOURNAL: LIEBIGS ANN CHEM 0 (1). 1989. 51-58. **1989**
FULL JOURNAL NAME: Liebigs Annalen der Chemie
CODEN: LACHD
RECORD TYPE: Abstract
LANGUAGE: GERMAN

ABSTRACT: In order to synthesize a variable system of well-defined one- and two-chain chiral amphiphiles that are able to form **liposomes**, we choose s-triazine as linking unit between the lipophilic and hydrophilic moieties. The lipophilic part is made of long-chain alcohols or **alkylmines**, whereas the hydrophillic part of the molecules is formed by the trifunctional amino acids L-**cysteine**, L-serine, or L-lysine. These are linked to the s-triazine with their .omega.-functional group. Because of the amino acid structure of the new lipids it is possible to examine their optical purity by thin-layer chromatography. On the investigation of their **liposome**-building properties only the **cysteine** amphiphiles with two **alkyl** chains are found to be capable of forming vesicles.

1989

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            $0.24    0.043 DialUnits File5
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            OneSearch, 2 files,  0.087 DialUnits FileOS
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     $0.38  Estimated total session cost   0.087 DialUnits

File 410:Chronolog(R)  1981-2002/Feb
       (c) 2002 The Dialog Corporation

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HILIGHT set on as ''
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     $0.00  Estimated cost this search
     $0.38  Estimated total session cost   0.159 DialUnits

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        (c) 2002 BIOSIS

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     $0.43  Estimated cost this search
     $0.81  Estimated total session cost   0.238 DialUnits

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  File   5:Biosis Previews(R)  1969-2002/Mar W3
        (c) 2002 BIOSIS

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         100322  CYSTEIN?
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? s s2 and py<1998

Processing
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      S3       19  S2 AND PY<1998
? s alkyl? and cystein?

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          100322  CYSTEIN?
      S4    3220  ALKYL? AND CYSTEIN?
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           49833  LIPOSOM?
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? rd

...completed examining records
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               6  S6
        20863023  PY<1998
      S7       5  S6 AND PY<1998
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 7/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08067600   91060585   PMID: 2246257
  Mitochondrial phosphate transport. N-ethylmaleimide insensitivity
correlates with absence of beef heart-like Cys42 from the Saccharomyces
cerevisiae phosphate transport protein.
  Guerin B; Bukusoglu C; Rakotomanana F; Wohlrab H
  Boston Biomedical Research Institute, Massachusetts.
  Journal of biological chemistry (UNITED STATES)   Nov 15 1990,  265
  (32)  p19736-41,  ISSN 0021-9258   Journal Code: HIV
  Contract/Grant No.: GM33357, GM, NIGMS
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  The mitochondrial phosphate transport protein (PTP) has been purified in
a reconstitutively active form from Saccharomyces cerevisiae and Candida
parapsilosis. ADP/ATP carriers that copurify have been identified. The PTP
from S. cerevisiae migrates as a single band (35 kDa) in sodium dodecyl
sulfate gels with the same mobility as the N-ethylmaleimide-alkylated
beef heart PTP. It does not cross-react with anti-sera against beef heart
PTP. The CNBr peptide maps of the yeast and beef proteins are very
different. The rate of unidirectional phosphate uptake into reconstituted
proteoliposomes is stimulated about 2.5-fold to a Vmax of 170 mumol of
phosphate min-1 (mg PTP)-1 (22 degrees C) by increasing the pHi of the
proteoliposomes from 6.8 (same as pHe) to 8.0. The Km for Pi of this
reconstituted activity is 2.2 mM. The transport is sensitive to mersalyl
(50% inhibition at 60 microM) and insensitive to N-ethylmaleimide. We have
purified peptides matching the highly conserved motif
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Pro-X-(Asp/glu)-X-X-(Lys/Arg)-X-(Arg/lys) (X is an unspecified amino acid) of the triplicate gene structure sequence of the beef heart PTP. The N-ethylmaleimide-reactive Cys42 of the beef heart protein, located between the two basic amino acids of this motif (Lys41-Cys42-Arg43), is replaced with a Thr in the yeast protein. This substitution most likely is responsible for the lack of N-ethylmaleimide sensitivity of the yeast protein and mersalyl thus reacts with another **cysteine** to inhibit the transport. Finally it is concluded that Cys42 has no essential role in the catalysis of inorganic phosphate transport by the mitochondrial phosphate transport protein.

7/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07165137 91227383 PMID: 1851304
An electron spin resonance study of merocyanine 540-mediated type I reactions in **liposomes**.
Feix JB; Kalyanaraman B
Department of Radiology, Medical College of Wisconsin, Milwaukee 53226.
Photochemistry and photobiology (ENGLAND) Jan **1991**, 53 (1) p39-45, ISSN 0031-8655 Journal Code: P69
Contract/Grant No.: CA-49089, CA, NCI; GM-22923, GM, NIGMS; RR-01008, RR, NCRR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The merocyanine 540 (MC540)-mediated reduction of nitroxide spin labels in a **liposomal** system was examined using electron spin resonance (ESR) spectroscopy. Spin label reduction was light driven, and occurred in **liposomes** composed of both fully-saturated (dimyristoyl) and mono-unsaturated (1-palmitoyl-2-oleoyl) phosphatidylcholine. Loss of the nitroxide ESR signal was enhanced by the physiological electron donors glutathione, **cysteine** , and NADPH; and was strongly inhibited by the presence of molecular oxygen. Nitroxides reduced in the presence of MC540 alone could be regenerated either by purging the sample with air or by the addition of ferricyanide, indicating that the ESR signal loss was due to reduction to the corresponding hydroxylamines. Only partial regeneration was attained for nitroxides reduced in the presence of glutathione, **cysteine** , or NADPH. Reduction rates for the lipophilic spin labels, 5-, 12-, and 16-doxyl stearic acid, were not influenced by the position of the nitroxide moiety along the **alkyl** chain, however reduction of spin labels occupying primarily the aqueous phase was much slower. These studies demonstrate that MC540 can initiate oxidation/reduction (Type I) reactions. Such Type I processes may augment the effects of singlet oxygen in MC540-mediated photodynamic therapy.

7/3,AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07501567 BIOSIS NO.: 000091075436
AN ESR STUDY OF MEROCYANINE 540-MEDIATED TYPE I REACTIONS IN **LIPOSOMES**
AUTHOR: FEIX J B; KALYANARAMAN B
AUTHOR ADDRESS: BIOPHYSICS SECT., DEP. RADIOL., MED. COLL. WIS., MILWAUKEE, WIS. 53266, USA.
JOURNAL: PHOTOCHEM PHOTOBIOL 53 (1). 1991. 39-46. **1991**
FULL JOURNAL NAME: Photochemistry and Photobiology
CODEN: PHCBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

? ds

Set	Items	Description
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S3	1	S1 AND N12 (W) BIS?
S4	0	S1 AND ?AMIDE?
S5	0	SPERMIN? AND ?AMIDE?
S6	0	LIPOSOM? AND CYSTEINAMIDE?
S7	21	CYSTEINAMIDE?
S8	19	RD (unique items)

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>>>File 155 processing for BIS? stopped at BISPOSPHONATES
>>>File 5 processing for BIS? stopped at BISFUNCTIONAL

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	112812	BIS?
S9	16	S1 AND BIS?

? rd

...completed examining records

S10	11	RD (unique items)

? t s10/3,ab/all

10/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11661265 21378180 PMID: 11485561

Polyamine analogues inhibit the ubiquitination of spermidine/**spermine** N1-acetyltransferase and prevent its targeting to the proteasome for degradation.

Coleman CS; Pegg AE
Department of Cellular and Molecular Physiology, The Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, P.O. Box 850, Hershey, PA 17033, USA. csc6@psu.edu

Biochemical journal (England) Aug 15 2001, 358 (Pt 1) p137-45, ISSN 0264-6021 Journal Code: 9YO
Contract/Grant No.: GM26290, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Spermidine/**spermine** N(1)-acetyltransferase (SSAT), a key enzyme in mammalian polyamine catabolism, undergoes rapid turnover (half-life approx. 30 min) and is highly inducible in response to polyamine analogues such as **bis**(ethyl)**spermine** (BE-3-4-3), which greatly stabilize the enzyme. Rapid degradation of SSAT in reticulocyte lysates was preceded by formation of a ladder of ubiquitinated forms, and required the production of high-molecular-mass complexes with ubiquitin (HMM-SSAT-Ubs). Mutation of all 11 lysines in SSAT separately to arginine demonstrated that no single lysine residue is critical for its degradation in vitro, but mutant K87R had a significantly longer half-life, suggesting that lysine-87 may be the preferred site for ubiquitination. Mutations at the C-terminus of SSAT, such as E171Q, resulted in marked stabilization of the protein, due to the lack of formation of the HMM-SSAT-Ubs. Addition of BE-3-4-3 prevented the accumulation of ubiquitin conjugates and the proteasomal degradation of wild-type SSAT. These results indicate that conformational changes brought about by the binding of polyamine analogues prevent the efficient polyubiquitination of SSAT, leading to a major increase in the amount of SSAT protein, and that alteration of the C-terminal end of the protein has a similar effect in preventing the productive interaction with an E2 or E3 component of the ubiquitin pathway.

10/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11574027 21273414 PMID: 11377090
In vitro cytotoxicity of glyco-S-nitrosothiols. a novel class of nitric oxide donors.
Babich H; Zuckerbraun HL
Department of Biology, Stern College for Women, Yeshiva University, 245 Lexington Avenue, New York 10016, New York, USA. babich@ymail.yu.edu
Toxicology in vitro (England) Jun 2001, 15 (3) p181-90, ISSN 0887-2333 Journal Code: DNS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The cytotoxicities of the nitric oxide (NO) donors, S-nitroso-N-acetylpencillamine (SNAP) and three glyco-SNAPs, glucose-1-SNAP, glucose-2-SNAP, and fructose-1-SNAP, towards the human gingival epithelioid S-G cell line and three human carcinoma cell lines derived from tissues of the oral cavity were compared using the neutral red (NR) assay. In general, the glucose-SNAPs were more cytotoxic than SNAP, which, in turn, was more cytotoxic than fructose-1-SNAP. Further studies focused on the response of S-G cells to glucose-2-SNAP. The cytotoxicity of glucose-2-SNAP was attributed to NO, as glucose-2-SNAP (t1/2=20 h at 28 degrees C) aged for 4 days was nontoxic, toxicity was eliminated in the presence of hydroxocobalamin, a specific NO scavenger, and toxicity was not noted with glucose-2-AP (the parent compound used to construct glucose-2-SNAP). Exposure of cells to glucose-2-SNAP resulted in a lessening of the intracellular level of glutathione and cells pretreated with the glutathione-depleter, 1,3-**bis**-(chloroethyl)-1-nitrosourea, were more sensitive to a subsequent challenge with glucose-2-SNAP. Cytotoxicity of glucose-2-SNAP was lessened upon coexposure with the antioxidants, myricetin, N-acetyl-L-**cysteine** , and L-ascorbic acid. S-G cells exposed to glucose-2-SNAP exhibited bi- and multinucleation. Death of S-G cells exposed to glucose-2-SNAP apparently occurred by apoptosis, as demonstrated with fluorescence microscopy by the appearance of brightly stained, hypercondensed chromatin in spherical cells and of membrane blebbing and by the DNA-ladder of oligonucleosome-length fragments noted with gel electrophoresis. In comparison with other classes of NO donors the sequence of toxicity towards S-G cells was S-nitrosoglutathione>glucose-SNAPs>SNAP, sodium nitroprusside>**spermine%% % NONOate>DPTA NONOate>DETA NONOate>fructose-1-SNAP>>SIN-1.**

10/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10852530 20404848 PMID: 10949915
Polyamines and thiols in the cytoprotective effect of L-cysteine and L-methionine on carbon tetrachloride-induced hepatotoxicity.
Chen W; Kennedy DO; Kojima A; Matsui-Yuasa I
Department of Food and Nutrition, Faculty of Human Life Science, Osaka City University, Osaka, Japan.
Amino acids (AUSTRIA) 2000, 18 (4) p319-27, ISSN 0939-4451 Journal Code: C77
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The relationship between cellular glutathione (GSH), protein-SH levels, and lactate dehydrogenase (LDH), with respect to the effect of polyamines on the cytoprotective ability of L-cysteine and L-methionine, the most important components in the sulfur amino acid metabolic pathway, in carbon tetrachloride (CCl4)-induced toxicity in isolated rat hepatocytes was studied. CCl4 induced a LDH release and decreased cellular thiols and

polyamines levels but treatment with L-cysteine and L-methionine reversed these decreases. Treating with methylglyoxal bis -(guanylhydrazone), MGBG, an irreversible inhibitor of S-adenosylmethionine decarboxylase, which is a key enzyme in spermidine and spermine biosynthesis, and therefore used to deplete cellular polyamines, prevented the protective effect of L-cysteine and L-methionine, but the addition of exogenous polyamines inhibited the influence of MGBG. These results suggest that the cytoprotective effect of L-cysteine and L-methionine in CCl4-induced toxicity were via maintenance of cellular polyamines, GSH and protein-SH concentrations and prevention of LDH leakage.

10/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10219685 99288824 PMID: 10361978
In vitro cytotoxicity of the nitric oxide donor, S-nitroso-N-acetyl-penicillamine, towards cells from human oral tissue.
Babich H; Zuckerbraun HL; Hirsch ST; Blau L
Department of Biology, Stern College for Women, Yeshiva University, New York, New York 10016, USA. babich@ymail.yu.edu
Pharmacology & toxicology (DENMARK) May 1999, 84 (5) p218-25, ISSN 0901-9928 Journal Code: PHT
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The cytotoxicity of the nitric oxide donor, S-nitroso-N-acetyl-penicillamine (SNAP), towards cultured human cells from oral tissue was evaluated. The toxicity of SNAP to Smulow-Glickman gingival epithelial cells was correlated with the liberation of nitric oxide, as N-acetyl-D,L-penicillamine, the SNAP metabolites, N-acetyl-D,L-penicillamine disulfide and nitrite, and preincubated (denitrosylated) SNAP did not affect viability. Comparing equimolar concentrations of various nitric oxide donors, cytotoxicity appeared to be inversely related to the relative stability (i.e., half-life) of the test compound; the sequence of cytotoxicity for a 4 hr exposure was S-nitrosoglutathione>>spermine NONOate> SNAP>DPTA NONOate>>DETA NONOate. Intracellular reduced glutathione (GSH) was lowered in S-G cells exposed to SNAP. Pretreatment of the cells with the GSH depleter, 1,3-bis-(chloroethyl)-1-nitrosourea (BCNU), enhanced the toxicity of SNAP Similar findings of enhanced sensitivity to SNAP were noted with gingival fibroblasts and periodontal ligament cells pretreated with BCNU. The toxicity of SNAP towards the gingival epithelial cells was decreased by cotreatment with the antioxidants, N-acetyl-L-cysteine , L-ascorbic acid, and (+)-catechin. Cells exposed to SNAP exhibited nuclear aberrations, including multilobed nuclei and multinucleation. SNAP-induced cell death was apparently by apoptosis, as noted by fluorescence microscopy and DNA agarose gel electrophoresis.

10/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09607253 98028689 PMID: 9359869
Rapid induction of apoptosis by deregulated uptake of polyamine analogues.
Hu RH; Pegg AE
Department of Cellular and Molecular Physiology, M.S. Hershey Medical Center, Pennsylvania State University College of Medicine 17033, USA.
Biochemical journal (ENGLAND) Nov 15 1997, 328 (Pt 1) p307-16, ISSN 0264-6021 Journal Code: 9YO
Contract/Grant No.: GM-26290, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
Treatment of Chinese hamster ovary cells with alpha-difluoromethylornithine for 3 days, followed by exposure to cycloheximide, led to an unregulated, rapid and massive accumulation of polyamine analogues. This accumulation led to cell death by apoptosis within a few hours. Clear evidence of DNA fragmentation was seen in response to both N-terminally ethylated polyamines and to polyamines containing methyl groups on the terminal carbon atoms. Programmed cell death was induced within 2-4 h of exposure to 1 &mgr;M or higher concentrations of N1,N11-bis (ethyl)norspermine. The presence of cycloheximide increased the uptake of the polyamine analogues and therefore led to cell death at lower analogue concentrations, but it was not essential for the induction of apoptosis, since similar effects were seen when the protein synthesis inhibitor was omitted and the concentration of N1, N11-bis(ethyl)norspermine was increased to 5 microM or more. The induction of apoptosis was blocked both by the addition of the caspase inhibitor N-benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone, or by the addition of the polyamine oxidase inhibitor N1-methyl-N2-(2,3-butadienyl)butane-1,4-diamine (MDL 72,527). These experiments provide evidence to support the concepts that: (1) polyamines or their oxidation products may be initiators of programmed cell death; (2) regulation of polyamine biosynthesis and uptake prevents the accumulation of toxic levels of polyamines; and (3) the anti-neoplastic effects of bis (ethyl) polyamine analogues may be due to the induction of apoptosis in sensitive tumour cells.

10/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09462818 97277366 PMID: 9115288
Proteasomal degradation of spermidine/spermine N1-acetyltransferase requires the carboxyl-terminal glutamic acid residues.
Coleman CS; Pegg AE
Department of Cellular and Molecular Physiology, The Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033, USA.
Journal of biological chemistry (UNITED STATES) May 2 1997, 272 (18) p12164-9, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM-26290, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The rapid turnover of spermidine/spermine N1-acetyltransferase (SSAT), a key enzyme in the regulation of polyamine levels, was found to be mediated via ubiquitination and the proteasomal system. SSAT degradation was blocked by the binding of polyamines or of the polyamine analog, N1,N12-bis(ethyl)spermine (BE-3-4-3), to the protein, providing a mechanism for the increase of SSAT activity in response to these agents. Site-directed mutagenesis indicated that a number of residues including arginine 19, cysteine 122, histidine 126, glutamic acid 152, arginine 155, and methionine 167 were needed for protection of SSAT by BE-3-4-3. These residues have previously been shown to reduce the affinity for the binding of polyamines to the SSAT protein, and these results indicate that the change in protein configuration brought about by this binding renders the protein resistant to proteasomal degradation. Mutations to alanines of residues arginine 7, cysteine 14, and lysine 141 also prevented the protection by BE-3-4-3, and these residues may be required for the formation of the protected conformation. The rapid degradation of SSAT required the carboxyl-terminal region of the protein, and the two terminal glutamic acid residues at positions 170 and 171 were found to be of critical importance. Truncation of the protein to remove these residues or the mutation of either of these acidic residues to glutamine completely abolished the rapid degradation of SSAT. The addition of two extra lysine

residues at the carboxyl terminus or the conversion of the glutamic acids at positions 170 and 171 to lysines also prevented SSAT degradation by the proteasome. These results show the key role of the acidic residues at the carboxyl terminus of the protein in reacting with the proteasome. In contrast, mutation of lysine 166 to alanine, which extends the length of the acidic region in the carboxyl-terminal fragment of SSAT, actually increased the rate of degradation of SSAT without affecting its stabilization by BE-3-4-3. The binding of BE-3-4-3 or polyamines is therefore likely to change the configuration of the SSAT protein in a way that prevents the exposure of the carboxyl-terminal region of the ubiquitinated protein to the proteasome.

10/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08866490 96179736 PMID: 8601724
Inhibition of polyamine synthesis alters hair follicle function and fiber composition.
Hynd PI; Nancarrow MJ
Department of Animal Science, University of Adelaide Waite Campus, Glen Osmond, South Australia, Australia.
Journal of investigative dermatology (UNITED STATES) Feb 1996, 106 (2) p249-53, ISSN 0022-202X Journal Code: IHZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The activities of ornithine decarboxylase and S-adenosylmethionine decarboxylase, two of the enzymes involved in the synthesis of the polyamines, were found to be high in follicle-rich homogenates of sheep skin, and to be responsive to the nutrition of the animal. Systemic provision of the inhibitor of ornithine decarboxylase, alpha difluoromethylornithine, markedly altered the length, diameter, and composition of the fiber, the last being accompanied by an increase in the proportion of the fiber occupied by paracortical cells and an increase in the level of mRNA encoding a cysteine -rich family of keratin proteins. The growth of wool follicles cultured in media containing alpha-difluoromethylornithine was not inhibited, even at high concentrations. In contrast, low concentrations of methylglyoxal (bis)guanylhydrazone, the inhibitor of S-adenosylmethionine decarboxylase, completely inhibited fiber growth in culture follicles. Addition of spermidine to the media overcame this inhibition but spermine had no effect. Further evidence that spermine is not required for normal follicle function was provided by incubating follicles with the specific inhibitor of spermine synthase, n-butyl-1,3-diaminopropane. This inhibitor, even at high concentrations, had no effect on fiber growth in vitro. Spermidine partially overcame the growth depression that occurred in follicles cultured in methionine-deficient media, suggesting that part of the requirement for methionine is for spermidine synthesis in the follicle. These investigations provide strong evidence that the polyamines in general , and spermidine in particular, play a major role in hair growth.

10/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08463988 95138106 PMID: 7836377
Detection and characterization of a transport system mediating cysteamine entry into human fibroblast lysosomes. Specificity for aminoethylthiol and aminoethylsulfide derivatives.
Pisoni RL; Park GY; Velilla VQ; Thoene JG
Department of Pediatrics and Communicable Diseases, University of Michigan Medical School, Ann Arbor 48109-2029.
Journal of biological chemistry (UNITED STATES) Jan 20 1995, 270 (3)

p1179-84, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: DK25548, DK, NIDDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The uptake of [3H]cysteamine by Percoll-purified human fibroblast lysosomes was investigated to determine whether lysosomes contain a transport system recognizing cysteamine. Lysosomal cysteamine uptake is a Na(+)-independent process which rapidly attains a steady state within 1 min at pH 7.0 and 37 degrees C. A biphasic Arrhenius plot is observed for cysteamine uptake, giving a Q10 of 2.2 from 17 to 26 degrees C and a Q10 of 1.2 from 27 to 35 degrees C. The rate of lysosomal cysteamine uptake is maximal at pH 8.2, half-maximal at pH 6.8, and declines approximately 50-fold from the maximum to show very little transport at pH 5.0. Cysteamine uptake into fibroblast lysosomes displays complete saturability with a Km of 0.88 mM and Vmax of 1410 pmol of beta-N-acetylhexosaminidase/min at pH 7.0 and 37 degrees C. Analog inhibition studies demonstrated that all analogs recognized thus far by the cysteamine carrier are either aminothiols or aminosulfides and contain an amino group and sulfur atom separated by a carbon chain, 2 carbon atoms in length. The Ki constants for these analogs as competitive inhibitors of lysosomal cysteamine uptake are 2-(ethylthio)ethylamine (0.64 mM), 1-amino-2-methyl-2-propanethiol (0.74 mM), 2-dimethylaminoethanethiol (0.87 mM), thiocholine (1.6 mM), and bis(2-aminoethyl)sulfide (4.9 mM). L-Cysteine , D-penicillamine, and analogs lacking either a sulfur atom or amino group are not recognized by the cysteamine carrier including ethanolamine, choline, taurine, beta-mercaptoethanol, ethylenediamine, cadaverine, spermine , spermidine, histamine, dopamine, and 3-hydroxytyramine. In a cystine-depletion assay, a 2-h exposure of cystinotic fibroblasts to 1 mM 1-amino-2-methyl-2-propanethiol lowers cell cystine levels to the same low level obtained with cysteamine. Thus, all four aminothiols, known to deplete cystinotic fibroblasts of their accumulated cystine, are recognized as substrates by the lysosomal cysteamine carrier, suggesting the importance of this transporter in the delivery of aminothiols to the lysosomal compartment.

10/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04764489 85030437 PMID: 6092366
Characterization of D-myo-inositol 1,4,5-trisphosphate phosphatase in rat liver plasma membranes.
Seyfred MA; Farrell LE; Wells WW
Journal of biological chemistry (UNITED STATES) Nov 10 1984, 259 (21) p13204-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AM 32930, AM, NIADDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

D-myo-Inositol 1,4,5-trisphosphate has been previously demonstrated to act as a second messenger for the hormonal mobilization of intracellular calcium in rat liver. In this study, the breakdown of D-myo-inositol 1,4,5-trisphosphate by a phosphatase activity was characterized. Using partially purified subcellular fractions, it was found that D-myo-inositol 1,4,5-trisphosphate phosphatase (I-P3ase) specific activity was highest in the plasma membrane fraction, while D-myo-inositol 1,4-bisphosphate phosphatase specific activity was highest in the cytosolic and microsomal fractions. The plasma membrane I-P3ase was Mg2+-dependent with optimal activity observed at 0.5-1.5 mM free Mg2+. The enzyme had a neutral pH optimum, suggesting that it was neither an acid nor alkaline phosphatase. Neither LiCl nor NaF inhibited the I-P3ase activity. However, both L-cysteine and dithiothreitol stimulated the activity 2-fold. Spermine (2.0 mM) inhibited the I-P3ase activity by 50%, while

putrescine and spermidine had little or no effect.

10/3,AB/10 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11456740 BIOSIS NO.: 199800238072
1!3C-NMR study of the potential role of spermine as a free radical scavenger.
AUTHOR: Sirisoma Nilantha S(a); Casero Robert A Jr; Casero Robert A Jr; Woster Patrick M(a)
AUTHOR ADDRESS: (a)Dep. Pharmaceutical Sci., Coll. Pharmacy and Allied Health, Wayne State Univ., Detroit, MI 48202**USA
JOURNAL: Abstracts of Papers American Chemical Society 215 (1-2):pMEDI 5 1998
CONFERENCE/MEETING: 215th American Chemical Society National Meeting Dallas, Texas, USA March 29-April 2, 1998
SPONSOR: American Chemical Society
ISSN: 0065-7727
RECORD TYPE: Citation
LANGUAGE: English
1998

10/3,AB/11 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02377315 BIOSIS NO.: 000065034346
S ADENOSYL METHIONINE METABOLISM AND ITS RELATION TO POLY AMINE SYNTHESIS IN RAT LIVER EFFECT OF NUTRITIONAL STATE ADRENAL FUNCTION SOME DRUGS AND PARTIAL HEPATECTOMY
AUTHOR: ELORANTA T O; RAINA A M
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. KUOPIO, P.O. BOX 138, SF-70101 KUOPIO 10, FINL.
JOURNAL: BIOCHEM J 168 (2). 1977 179-186. 1977
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: S-Adenosylmethionine metabolism and its relation to the synthesis and accumulation of polyamines was studied in rat liver under various nutritional conditions, in adrenalectomized or partially hepatectomized animals and after treatment with cortisol, thioacetamide or methylglyoxal bis(guanylhydrazone) {1,1'-[(methylethanediylidine)dinitriol]diguanidine}. Starvation for 2 days only slightly affected S-adenosylmethionine metabolism. The ratio of spermidine/spermine decreased markedly, but the concentration of total polyamines did not change significantly. The activity of S-adenosylmethionine decarboxylase initially decreased and then increased during prolonged starvation. This increase was dependent on intact adrenals. Re-feeding of starved animals caused a rapid but transient stimulation of polyamine synthesis and also increased the concentrations of S-adenosylmethionine and S-adenosylhomocysteine. Cortisol treatment enhanced the synthesis of polyamines, S-adenosylmethionine and S-adenosylhomocysteine. Feeding with a methionine-deficient diet for 7-14 days profoundly increased the concentration of spermidine, whereas the concentrations of total polyamines and of S-adenosylmethionine showed no significant changes. The results show that nutritional state and adrenal function play a significant role in the regulation of hepatic metabolism of S-adenosylmethionine and polyamines. They indicate that under a variety of physiological and experimental conditions the concentrations

of S-adenosylmethionine and of total polyamines remain fairly constant and that changes in polyamine metabolism are not primarily connected with changes in the accumulation of S-adenosylmethionine or S-adenosylhomocysteine.

1977

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 b 155, 5

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  File   5:Biosis Previews(R)  1969-2002/Mar W3
         (c) 2002 BIOSIS

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          100322  CYSTEIN?
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             240  N12
           64581  BIS
              69  N12(W)BIS
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 3/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09462818   97277366   PMID: 9115288
  Proteasomal degradation of spermidine/spermine N1-acetyltransferase
requires the carboxyl-terminal glutamic acid residues.
  Coleman CS; Pegg AE
  Department of Cellular and Molecular Physiology, The Milton S. Hershey
Medical Center, Pennsylvania State University College of Medicine, Hershey,
Pennsylvania 17033, USA.
  Journal of biological chemistry (UNITED STATES)   May 2 1997,  272  (18)
 p12164-9,  ISSN 0021-9258   Journal Code: HIV
  Contract/Grant No.: GM-26290, GM, NIGMS
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  The rapid turnover of spermidine/spermine N1-acetyltransferase
(SSAT), a key enzyme in the regulation of polyamine levels, was found to be
mediated via ubiquitination and the proteasomal system. SSAT degradation
was blocked by the binding of polyamines or of the polyamine analog, N1,
N12-bis(ethyl)spermine   (BE-3-4-3),   to   the   protein,
providing a mechanism for the increase of SSAT activity in response to
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these agents. Site-directed mutagenesis indicated that a number of residues including arginine 19, **cysteine** 122, histidine 126, glutamic acid 152, arginine 155, and methionine 167 were needed for protection of SSAT by BE-3-4-3. These residues have previously been shown to reduce the affinity for the binding of polyamines to the SSAT protein, and these results indicate that the change in protein configuration brought about by this binding renders the protein resistant to proteasomal degradation. Mutations to alanines of residues arginine 7, **cysteine** 14, and lysine 141 also prevented the protection by BE-3-4-3, and these residues may be required for the formation of the protected conformation. The rapid degradation of SSAT required the carboxyl-terminal region of the protein, and the two terminal glutamic acid residues at positions 170 and 171 were found to be of critical importance. Truncation of the protein to remove these residues or the mutation of either of these acidic residues to glutamine completely abolished the rapid degradation of SSAT. The addition of two extra lysine residues at the carboxyl terminus or the conversion of the glutamic acids at positions 170 and 171 to lysines also prevented SSAT degradation by the proteasome. These results show the key role of the acidic residues at the carboxyl terminus of the protein in reacting with the proteasome. In contrast, mutation of lysine 166 to alanine, which extends the length of the acidic region in the carboxyl-terminal fragment of SSAT, actually increased the rate of degradation of SSAT without affecting its stabilization by BE-3-4-3. The binding of BE-3-4-3 or polyamines is therefore likely to change the configuration of the SSAT protein in a way that prevents the exposure of the carboxyl-terminal region of the ubiquitinated protein to the proteasome.
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 8/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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11687785 21412078 PMID: 11520197
Synthesis, molecular modeling, and structure-activity relationship of benzophenone-based CAAX-peptidomimetic farnesyltransferase inhibitors.
Sakowski J; Bohm M; Sattler I; Dahse HM; Schlitzer M
Institut fur Pharmazeutische Chemie, Philipps-Universitat Marburg, Marbacher Weg 6, D-35032 Marburg, Germany.
Journal of medicinal chemistry (United States) Aug 30 2001, 44 (18) p2886-99, ISSN 0022-2623 Journal Code: J0F
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Because of the involvement of farnesylated proteins in oncogenesis, inhibition of the protein-modifying enzyme farnesyltransferase is considered a major emerging strategy in cancer therapy. Here, we describe the structure-activity relationship of a novel class of CAAX-peptidomimetic farnesyltransferase inhibitors based on the benzophenone scaffold. 4'-Methyl, 4'-chloro, 4'-bromo, and 4'-nitrophenylacetic acid as substituents at the 2-amino group of the benzophenone core structure yield farnesyltransferase inhibitors active in the nanomolar range. Using diphenylacetic acid in this position further improves activity. SEAL superimposition of inhibitor 12a to the enzyme-bound conformation of a CAAX-peptide shows a markedly good resemblance of the molecular properties of the peptide. FlexX docking of 12a confirms the good fit of the molecule into the peptide binding site of farnesyltransferase. The novel benzophenone-based AAX-peptidomimetic substructure described here will be useful for the design of some novel types of farnesyltransferase inhibitors.

8/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10930588 21036734 PMID: 11196190
Matrix metalloproteinase 2 in tumor cell-induced platelet aggregation: regulation by nitric oxide.
Jurasz P; Sawicki G; Duszyk M; Sawicka J; Miranda C; Mayers I; Radomski MW
Department of Pharmacology, University of Alberta, Edmonton, Canada.
Cancer research (United States) Jan 1 2001, 61 (1) p376-82, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A correlation exists between the ability of tumor cells to aggregate platelets and their tendency to metastasize. Tumor cell-induced platelet aggregation (TCIPA) facilitates the embolization of the vasculature with tumor cells and the formation of metastatic foci. It is well documented that matrix metalloproteinases (MMPs) play an integral part in tumor spread and the metastatic cascade. Therefore, we have examined the role of MMPs during TCIPA and its regulation by nitric oxide (NO) in vitro. Human HT-1080 fibrosarcoma and A549 lung epithelial cancer cells induced TCIPA in a concentration-dependent manner that was monitored by aggregometry. This aggregation resulted in the release of MMIP-2 from platelets and cancer cells, as measured by zymography. HT-1080 cells released significantly more MMP-2 than A549 cells and were more efficacious in inducing TCIPA. Inhibition of MMP-2 with phenanthroline (1-1000 microM), a synthetic inhibitor of MMPs, and by neutralizing anti-MMIP-2 antibody (10 microg/ml) reduced TCIPA induced by HT-1080 cells. TCIPA was abolished by simultaneous inhibition of platelet function with acetylsalicylic acid (100 microM; thromboxane pathway inhibitor), apyrase (250 microg/ml; ADP pathway inhibitor), and phenanthroline. NO donors such as S-nitroso-n-acetylpenicillamine and S-nitrosoglutathione (both at 0.01-100 microM) inhibited TCIPA and MMP-2 release from platelets and tumor cells.

The inhibitory actions of S-nitroso-n-acetylpenicillamine and S-nitrosoglutathione were reversed by 1H-[1,2,4]oxadiazole[4,3]quinoxalin-1-one (0.01-30 microM), a selective inhibitor of the soluble guanylyl cyclase. We conclude that (a) human fibrosarcoma cells aggregate platelets via mechanism(s) that are mediated, in part, by MMP-2; (b) NO inhibits TCIPA, in part, by attenuating the release of MMP-2; and (c) these effects of NO are cGMP-dependent.

8/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10210386 99308982 PMID: 10381252
Vanadium: a review of its potential role in the fight against diabetes.
Badmaev V; Prakash S; Majeed M
Sabinsa Corporation, Piscataway, New Jersey 08854, USA. sabinsa@compuserve.com
journal of alternative and complementary medicine (UNITED STATES) Jun 1999, 5 (3) p273-91, ISSN 1075-5535 Journal Code: CY7
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
The potential role of vanadium in human health is described as a building material of bones and teeth. However, another very interesting and promising application for vanadium in human health emerges from recent studies that evaluated the role of vanadium in the management of diabetes. Vanadium is present in a variety of foods that we commonly eat. Skim milk, lobster, vegetable oils, many vegetables, grains and cereals are rich source of vanadium (>1 ppm). Fruits, meats, fish, butter, cheese, and beverages are relatively poor sources of vanadium. The daily dietary intake in humans has been estimated to vary from 10 microg to 2 mg of elemental vanadium, depending on the environmental sources of this mineral in the air, water, and food of the particular region tested. In animals, vanadium has been shown essential (1-10 microg vanadium per gram of diet). There is only circumstantial evidence that vanadium is essential for humans. However, in doses ranging from 0.083 mmol/d to 0.42 mmol/d, vanadium has shown therapeutic potential in clinical studies with patients of both insulin-dependent diabetes mellitus (IDDM) and noninsulin-dependent diabetes mellitus (NIDDM) type. Although vanadium has a significant biological potential, it has a poor therapeutic index, and attempts have been made to reduce the dose of vanadium required for therapeutic effectiveness. Organic forms of vanadium, as opposed to the inorganic sulfate salt of vanadium, are recognized as safer, more absorbable, and able to deliver a therapeutic effect up to 50% greater than the inorganic forms. The goal is to provide vanadium with better gastrointestinal absorption, and in a form that is best able to produce the desired biological effects. As a result, numerous organic complexes of vanadium have been developed including bis(maltolato)oxovanadium (BMOV), bis(**cysteinamide** N-octyl)oxovanadium known as Naglivan, bis(pyrrolidine-N-carbodithioato)oxovanadium, vanadyl-cysteine methyl ester, and bis-glycinato oxovanadium (BGOV). The health benefits of vanadium and the safety and efficacy of the available vanadium supplements are discussed in this review.

8/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08775235 95379558 PMID: 7651199
Measurement of glutathione redox state in cytosol and secretory pathway of cultured cells.
Hwang C; Lodish HF; Sinskey AJ
Genzyme Corporation, Framingham, Massachusetts 01701, USA.
Methods in enzymology (UNITED STATES) 1995, 251 p212-21, ISSN

0076-6879 Journal Code: MVA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

8/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08155367 94218912 PMID: 8165652
Antithrombotic effects and bleeding time prolongation with synthetic platelet GPIIb/IIIa inhibitors in animal models of platelet-mediated thrombosis.
Collen D; Lu HR; Stassen JM; Vreys I; Yasuda T; Bunting S; Gold HK
Center for Thrombosis and Vascular Research, University of Leuven, Belgium.
Thrombosis and haemostasis (GERMANY) Jan 1994, 71 (1) p95-102, ISSN 0340-6245 Journal Code: VQ7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cyclic Arg-Gly-Asp (RGD) containing synthetic peptides such as L-cysteine, N-(mercaptoacetyl)-D-tyrosyl-L-arginylglycyl-L-alpha-aspartyl-cyclic (1-->5)-sulfide, 5-oxide (G4120) and acetyl-L-cysteinyl-L-asparaginyl-L-propyl-L-arginyl-glycyl-L-alpha- aspartyl-[0-methyltyrosyl]-L-arginyl-L-**cysteinamide** , cyclic 1-->9-sulfide (TP9201) bind with high affinity to the platelet GPIIb/IIIa receptor. The relationship between antithrombotic effect, ex vivo platelet aggregation and bleeding time prolongation with both agents was studied in hamsters with a standardized femoral vein endothelial cell injury predisposing to platelet-rich mural thrombosis, and in dogs with a carotid arterial eversion graft inserted in the femoral artery. Intravenous administration of G4120 in hamsters inhibited in vivo thrombus formation with a 50% inhibitory bolus dose (ID50) of approximately 20 micrograms/kg, ex vivo ADP-induced platelet aggregation with ID50 of 10 micrograms/kg, and bolus injection of 1 mg/kg prolonged the bleeding time from 38 +/- 9 to 1,100 +/- 330 s. Administration of TP9201 in hamsters inhibited in vivo thrombus formation with ID50 of 30 micrograms/kg, ex vivo platelet aggregation with an ID50 of 50 micrograms/kg and bolus injection of 1 mg/kg did not prolong the template bleeding time. In the dog eversion graft model, infusion of 100 micrograms/kg of G4120 over 60 min did not fully inhibit platelet-mediated thrombotic occlusion but was associated with inhibition of ADP-induced ex vivo platelet aggregation and with prolongation of the template bleeding time from 1.3 +/- 0.4 to 12 +/- 2 min.(ABSTRACT TRUNCATED AT 250 WORDS)

8/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07180397 92412067 PMID: 1530602
Conformational study of cyclo(1,5)-Ac-Pen-Arg-Gly-Asp-Cys-NH2 in water by NMR and molecular dynamics.
Siahaan TJ; Chakrabarti S; Vander Velde D
Pharmaceutical Chemistry Department, University of Kansas, Lawrence 66045.
Biochemical and biophysical research communications (UNITED STATES) Sep 16 1992, 187 (2) p1042-7, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cyclo(1,5)-Ac-Pen-Arg-Gly-Asp-Cys-NH2 (3) is a potent inhibitor of platelet aggregation. Nuclear magnetic resonance (NMR) and restrained molecular dynamics were used to study the conformations of 3. Elucidation of RGD conformations in 3 will increase the understanding of interaction

between the RGD-sequence with GPIIb/IIIa.

8/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06017475 88107626 PMID: 3322393
Possible involvement of the A20-A21 peptide bond in the expression of the biological activity of insulin. 1. [21-Desasparagine,20-**cysteinamide** -A]insulin and [21-desasparagine,20-cysteine isopropylamide-A]insulin.
Chu YC; Wang RY; Burke GT; Chanley JD; Katsoyannis PG
Department of Biochemistry, Mount Sinai School of Medicine of the City University of New York, New York 10029.
Biochemistry (UNITED STATES) Nov 3 1987, 26 (22) p6966-71, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: DK-12925, DK, NIDDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The C-terminal region of the A chain of insulin has been shown to play a significant role in the expression of the biological activity of the hormone. To further delineate the contribution of this segment, we have synthesized [21-desasparagine,20-**cysteinamide** -A]insulin and [21-desasparagine,20-cysteine isopropylamide-A]insulin, in which the C-terminal amino acid residue of the A chain of insulin, asparagine, has been removed and the resulting free carboxyl group of the A20 cysteine residue has been converted to an amide and an isopropylamide, respectively. Both insulin analogues display biological activity, 14-15% for the unsubstituted amide analogue and 20-22% for the isopropylamide analogue, both relative to bovine insulin. In contrast, a [21-desasparagine-A]insulin analogue has been reported to display less than 4% of the activity of the natural hormone [Carpenter, F. (1966) Am. J. Med. 40, 750-758]. The implications of these findings are discussed, and we conclude that the A20-A21 amide bond plays a significant role in the expression of the biological activity of insulin.

8/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04826071 85014933 PMID: 6207538
Human placental syncytiotrophoblastic Mr 75,000 polypeptide defined by antibodies to a synthetic peptide based on a cloned human endogenous retroviral DNA sequence.
Suni J; Narvanen A; Wahlstrom T; Aho M; Pakkanen R; Vaheri A; Copeland T; Cohen M; Oroszlan S
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Oct 1984, 81 (19) p6197-201, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: 1-CO-23909-LB1, CO, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Antibodies to a synthetic undecapeptide (NH2-Cys-Glu-Asn-Pro-Ser-Gln-Phe-Tyr-Glu-Arg-Leu-COOH), the sequence (except cysteine) of which was deduced from a previously reported cloned human retroviral gag-gene-related DNA sequence erv-1, were raised in rabbits. In immunohistochemical staining these antibodies reacted with normal human first-trimester placentas and with blighted ova and benign and malignant trophoblastic tumors (hydatidiform and destructive moles, choriocarcinomas) but not with any other normal embryonic or adult tissues tested. In all tissues the reactivity was mainly confined to cells with trophoblastic morphology. In immunoblotting the antibody detected an Mr 75,000 polypeptide in syncytiotrophoblasts isolated from first-trimester placentas and in three

different lines of cultured choriocarcinoma cells. The undecapeptide blocked the reactivity of the antibody.

8/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

00604894 68313126 PMID: 5658546
Kinetic studies at high pH of the trypsin-catalyzed hydrolysis of N-alpha-benzoyl derivatives of L-arginamide, L-lysinamide, and S-2-aminoethyl-L-**cysteinamide** and related compounds.
Wang SS; Carpenter FH
Journal of biological chemistry (UNITED STATES) Jul 10 1968, 243 (13) p3702-10, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

8/3,AB/10 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13064353 BIOSIS NO.: 200100271502
Allylic protection of thiols and cysteine. III. Use of Fmoc-Cys(Fsam)-OH for solid-phase peptide synthesis.
AUTHOR: Gomez-Martinez Paloma; Guibe Francois(a); Albericio Fernando
AUTHOR ADDRESS: (a)Laboratoire de Catalyse Moleculaire, Institut de Chimie Moleculaire d'Orsay, UPRESA-8075, Universite Paris-Sud, Bat 420, F-91405, Orsay: albericio@qo.ub.es**France
JOURNAL: Letters in Peptide Science 7 (4):p187-194 2000
MEDIUM: print
ISSN: 0929-5666
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The solid-phase synthesis of peptides containing Cys has been carried out using the new thiol protecting group Fsam, which is completely stable to basic and acidic conditions used in both main strategies and can be selectively removed by palladium-catalyzed allylic cleavage in the presence of nucleophiles. This protecting group adds a new dimension of orthogonality for regioselective cysteine pairing strategies.

2000

8/3,AB/11 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10524663 BIOSIS NO.: 199699145808
Structural characterisation of acetaldehyde adducts formed by a synthetic peptide mimicking the N-terminus of the hemoglobin beta-chain under reducing and nonreducing conditions.
AUTHOR: Sillanaukee Pekka(a); Hurme Liisa; Tuominen Jari; Ranta Esko; Nikkari Seppo; Seppa Kaija
AUTHOR ADDRESS: (a)Alcohol Related Dis., Pharm. Upjohn Diagnostics, S-751 82 Uppsala**Sweden
JOURNAL: European Journal of Biochemistry 240 (1):p30-36 1996
ISSN: 0014-2956
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: This work was carried out to elucidate the structures resulting from acetaldehyde-induced modifications at the haemoglobin beta-chain N-terminal residues under different experimental conditions. A synthetic peptide (Val-His-Leu-Thr-Pro-Glu-Cys) of m/z 798, which represents the six N-terminal residues of the haemoglobin beta-chain N-terminus with an additional C-terminal cysteine, was used as a model compound. Peptide-acetaldehyde adducts were separated by reverse-phase HPLC. Fast-atom-bombardment MS and linked-scan (B/E) spectra were used to study adduct structures. Under nonreducing conditions at pH 7.4 (1:10 peptide/acetaldehyde molar ratio),. two types of adducts of m/z 824 were formed, both with modifications at the N-terminal valine. These two adducts were shown to be a Schiff base, and a cyclic 2-methyl-imidazolidine-4-one. The 2-methyl-imidazolidine-4-one adduct was demonstrated to be formed via the Schiff base and to undergo dissociation gradually after 24 h. Reducing conditions at pH 7.4 (peptide/acetaldehyde molar ratio of 1:1 with 20 mM NaCNBH-3) resulted in the formation of an adduct of m/z 826, which was shown to be an N-ethylated adduct of valine. A small amount of nonreduced adducts were also formed under these conditions. Reducing conditions at pH 9.0 (1:10 peptide/acetaldehyde molar ratio with 20 mM NaCNBH-3) yielded two secondary, i.e. diethylated (m/z 854), products very rapidly. The cysteine residue of the peptide was not found to form an adduct with acetaldehyde under physiological pH.

1996

8/3,AB/12 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07001404 BIOSIS NO.: 000038096320
EFFECT OF THE SOMATOSTATIN ANALOGUE SMS-201-995 ON FECAL FAT EXCRETION IN ACROMEGALY
AUTHOR: MCGREGOR A R; TROUGHTON W D; DONALD R A; ESPINER E A
AUTHOR ADDRESS: DEP. ENDOCRINOL., PRINCESS MARGARET HOSP., CASHMERE ROAD, CHRISTCHURCH 2, NEW ZEALAND.
JOURNAL: HORM METAB RES 22 (1). 1990. 55-56. 1990
FULL JOURNAL NAME: Hormone and Metabolic Research
CODEN: HMMRA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1990

8/3,AB/13 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04533757 BIOSIS NO.: 000029056794
EFFECT OF LONG-ACTING SOMATOSTATIN-ANALOG SMS-201995 D PHENYLALANYL-L-CYSTEINYL-L-PHENYLALANYL-D-TRYPTOPHYL-L-LYSYL-L-THREONYL-N-2-HYDROXY-1-HYDROXYMETHYLPROPYL-L-**CYSTEINAMIDE** CYCLIC 2-7 DISULFIDE ON GUT HORMONE SECRETION IN NORMAL SUBJECTS
AUTHOR: KRAENZLIN M E; WOOD S M; NEUFELD M; ADRIAN T E; BLOOM S R
AUTHOR ADDRESS: DEP. MED., HAMMERSMITH HOSP., LONDON, ENGL., UK.
JOURNAL: EXPERIENTIA (BASEL) 41 (6). 1985. 738-740. 1985
FULL JOURNAL NAME: EXPERIENTIA (Basel)
CODEN: EXPEA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1985

8/3,AB/14 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04387499 BIOSIS NO.: 000028020540
LONG-ACTING AND SELECTIVE SUPPRESSION OF GROWTH HORMONE SECRETION BY SOMATOSTATIN ANALOG SMS-201-995 D PHENYLALANYL-L-CYSTEINYL-L-PHENYLALANYL-D-TRYPTOPHYL-L-LYSYL-L-THREONYL-N -2-HYDROXY-1-HYDROXYMETHYLPROPYL-L-**CYSTEINAMIDE** CYCLIC 2-7-DISULFIDE IN ACROMEGALY
AUTHOR: PLEWE G; BEYER J; KRAUSE U; NEUFELD M; DEL POZO E
AUTHOR ADDRESS: DEP. ENDOCRINOLOGY, SCH. MED., UNIV. MAINZ, LANGENBECKSTR. 1, D-6500 MAINZ, GER.
JOURNAL: LANCET 2 (8406). 1984. 782-784. 1984
FULL JOURNAL NAME: Lancet
CODEN: LANCA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1984

8/3,AB/15 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04067580 BIOSIS NO.: 000026060640
EFFECTS ON BLOOD GLUCOSE IN RATS AND RHESUS MONKEYS OF A NEW HIGHLY ACTIVE ANALOG OF SOMATOSTATIN SMS-201-995
AUTHOR: DOEPFNER W; BRINER U; MARBACH P
AUTHOR ADDRESS: PRECLIN. RES. DEP., SANDOZ LTD., CH 4002 BASEL, SWITZERLAND.
JOURNAL: 14TH ACTA ENDOCRINOLOGICA CONGRESS, STOCKHOLM, SWEDEN, JUNE 27-30, 1983. ACTA ENDOCRINOL 103 (256). 1983. 79. 1983
CODEN: ACEDA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1983

8/3,AB/16 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03966236 BIOSIS NO.: 000076051802
SYNTHESIS OF L CYSTEINE DERIVATIVES OF IMMUNOTROPIC ACTIVITY
AUTHOR: KWAPISZEWSKI W; ILIASZENKO J; SOKOLOWSKA-MUSZYNSKA M
AUTHOR ADDRESS: DEP. PHARMACEUTICAL CHEMISTRY, INSTITUTE DRUG SCI., MED. ACADEMY, BANACHA 1, 02-097 WARSAW.
JOURNAL: ARCH IMMUNOL THER EXP 29 (6). 1981 (RECD. 1983). 823-826. 1981
FULL JOURNAL NAME: Archivum Immunologiae et Therapiae Experimentalis
CODEN: AITEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In a continued search for new compounds with immunotropic and anti-inflammatory activity, synthesis of 7 new derivatives of L-cysteine, S-methyl-N-acetylcysteine amide, hydrazide and acetylhydrazide, S-methyl-N-acetylcysteine methylhydrazide, [S-methyl-N-acetylcysteine N-methyl-N-acetyl-hydrazide], S-methylcysteine morpholineamide [hydrobromide] and S-methyl-N-acetylcysteine morpholineamide, was developed. In general the syntheses consisted of obtaining esters of

cysteine and S-methylcysteine, which were submitted to aminolysis and the obtained derivatives were acetylated with acetic anhydride. S-Methylcysteine morpholineamides were obtained by condensation of morpholine with cysteine derivatives by carbodiimied and/or mixed anhydride method. Yields of the compounds were high. Elemental composition was confirmed by elementary analysis.

1981

8/3,AB/17 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03938005 BIOSIS NO.: 000076023571
CYCLIC PEPTIDE DI SULFIDES SOLUTION AND SOLID STATE CONFORMATION OF N-TERT BUTOXYCARBONYL-L-CYSTEINYL-L-PROLYL-ALPHA-AMINOISOBUTYRYL-N-METHYL-L **CYSTEINAMIDE** CYCLIC DI SULFIDE A DI SULFIDE BRIDGED PEPTIDE HELIX
AUTHOR: RAVI A; PRASAD B V V; BALARAM P
AUTHOR ADDRESS: MOLECULAR BIOPHYSICS UNIT, INDIAN INSTITUTE SCI., BANGALORE 560 012, INDIA.
JOURNAL: J AM CHEM SOC 105 (1). 1983. 105-109. 1983
FULL JOURNAL NAME: Journal of the American Chemical Society
CODEN: JACSA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The solution and solid-state conformations of the peptide disulfide .**GRAPHIC**. [Boc = tert-butyloxycarbonyl, Aib = .alpha.-aminoisobutyric acid] were determined by NMR spectroscopy and X-ray diffraction. The Cys(4) and methylamide NH groups are solvent shielded in CDCl3 and (CD3)2SO, suggesting their involvement in intramolecular H-bonding. On the basis of known stereochemical preferences of Pro and Aib residues, a consecutive .beta.-turn structure is favored in solution. X-ray diffraction analysis reveals a highly folded 310 helical conformation for the peptide, with the S-S bridge lying approximately parallel to the helix axis, linking residues 1 and 4. The backbone conformational angles are Cys(1) .vphi. = -121.1.degree., .psi.= 65.6.degree.; Pro(2) .vphi. = -58.9.degree., .psi. = 34..degree.; Aib(3) .vphi. = -61.8.degree., .psi. = -17.9.degree.; Cys(4) .vphi. = 70.5.degree., .psi. = -18.6.degree.. Two intramolecular H-bonds are observed between Cys(1) CO.sbd.HN Cys(4) and Pro(2) CO.sbd.HNMe. The S.sbd.S bond has a right-handed chirality, with a dihedral angle (.chi.SS) of 82.degree..

1983

8/3,AB/18 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03928912 BIOSIS NO.: 000076014478
FORMATION BY HYDROGEN PER OXIDE OR 254 NANOMETER RADIATION OF A NEAR UV CHROMOPHORE FROM PEPTIDE BOUND CYSTEINE
AUTHOR: MCCORMICK J P; KLITA S; TERRY J; SCHRODT M; EISENSTARK A
AUTHOR ADDRESS: DEP. CHEM. DIV. BIOL. SCI., UNIV. MISSOURI, COLUMBIA, MO. 65211, USA.
JOURNAL: PHOTOCHEM PHOTOBIOL 36 (3). 1982. 367-370. 1982
FULL JOURNAL NAME: Photochemistry and Photobiology
CODEN: PHCBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Treatment of glutathione or N-acetylcysteinamide in water with H2O2, or with 254 nm radiation together with molecular O2, results in the formation of a near-UV chromophore having maximal absorption at 305 nm. From examination of related compounds, it is apparent that the N-acylcysteinamide residue is the key element required for generation of the 305 nm chromophore. The structure of this near-UV chromophore is stable to base but unstable in aqueous acid, is relatively sensitive to oxidation by H2O2 but is only very slowly reduced by sodium borohydride and displays good thermal stability at 50.degree. C.

1982

8/3,AB/19 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03153580 BIOSIS NO.: 000021031695
IN-VIVO AND IN-VITRO EFFECTS OF SERUM FACTOR AND RELATED COMPOUNDS ON HEPATOCYTE PROLIFERATION
AUTHOR: KOJI T; MIYAMOTO-MORIOKA M; TERAYAMA H
AUTHOR ADDRESS: ZOOL. INST., FAC. SCI., UNIV. TOKYO, TOKYO 113.
JOURNAL: 33RD ANNUAL MEETING OF THE JAPAN SOCIETY FOR CELL BIOLOGY, TOKYO, JAPAN, NOV. 13-15, 1980. CELL STRUCT FUNCT 5 (4). 1980 (RECD. 1981). 398.
1980
CODEN: CSFUD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1980

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Set     Items   Description
S1        115   SPERMINE AND CYSTEIN?
S2          1   S1 AND N12 (W) BIS
S3          1   S1 AND N12 (W) BIS?
S4          0   S1 AND ?AMIDE?
S5          0   SPERMIN? AND ?AMIDE?
S6          0   LIPOSOM? AND CYSTEINAMIDE?
S7         21   CYSTEINAMIDE?
S8         19   RD (unique items)
S9         16   S1 AND BIS?
S10        11   RD (unique items)
? s s1 not s2-s10

             115  S1
               1  S2
               1  S3
               0  S4
               0  S5
               0  S6
              21  S7
              19  S8
              16  S9
              11  S10
     S11      99  S1 NOT S2-S10
? rd

...examined 50 records  (50)
...completed examining records
     S12      78  RD (unique items)
? t s12/3,ab/all


 12/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12730480   21648498   PMID: 11788780
  Induction     of     metallothionein-I     protects     glomeruli     from
superoxide-mediated increase in albumin permeability.
  Sharma Ram; Sharma Mukut; Datta Prasun K; Savin Virginia J
  Department  of  Medicine,  Division  of  Nephrology,  Medical  College  of
Wisconsin, Milwaukee, Wisconsin 53226, USA.
  Experimental  biology  and medicine (Maywood, N.J.) (United States)   Jan
2002,  227  (1)  p26-31,  ISSN 1535-3702   Journal Code: 100973463
  Contract/Grant No.: R01 AM-22040, AM, NIADDK
  Languages: ENGLISH
  Document type: Journal Article
  Record type: In Process
  Metallothioneins     (MT)     are     low-molecular-weight,     heat-stable,
cysteine -rich proteins with four isoforms. MT-I and MT-II are
ubiquitous  and  are  induced  by oxidative, physical, and chemical stress.
MT-I  is  an  efficient  scavenger  of  superoxide  (*O2)  and hydroxyl ion
(OH(-)).  We  have  demonstrated  that *O2 and hypohalous acid can cause an
increase  in glomerular albumin permeability (P(alb)) in vitro. The purpose
of  this  study was to document the protective effect of MT gene product on
the  *O2-mediated increase in P(alb). Glomeruli from Sprague-Dawley rats in
4%  BSA  medium were incubated for 4 hr at 37 degrees C in duplicate tubes.
Each  set  contained  glomeruli  alone  or  with  5  microM  Cd(++), 0.3 mM
Spermine -NONOate  (NO  donor),  0.3  mM Sulfo-NONOate (nitrous oxide
donor),  0.6  mM  SNP  (nonspecific  NO  donor)  and SNP + carboxy-PTIO (10
mg/ml).  After  incubation,  one set of tubes was used to isolate total RNA
for  the  measurement  of  the mRNA levels of MT-I by reverse transcriptase
polymerase  chain  reaction (RT-PCR). Duplicate tubes were incubated for an
additional  10  min  with 10 nM of *O2, and P(alb) was measured using video
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microscopy. RT-PCR of total RNA from Cd(++) and Spermine-NONOate treated glomeruli revealed a 2-fold induction of MT-I expression at the mRNA level. *O2 caused a significant increase in P(alb) (0.8 +/- 0.06 vs. control 0.0 +/- 0.12, P < 0.05) and induction of MT-I in glomeruli by Cd(++) or by Spermine-NONOate blocked this effect (0.21 +/- 0.12 and 0.24 +/- 0.19, respectively, P < 0.05 vs. *O2). In contrast, Sulfo-NONOate and SNP did not induce mRNA for MT-I in glomeruli and did not provide protection against *O2-mediated increase in P(alb.) We conclude that MT-I gene products may play an important role in protecting the glomerular filtration barrier from the injury induced by reactive oxygen species in immune and/or nonimmune renal diseases.

12/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11772922 21446562 PMID: 11562201
Dimerizable cationic detergents with a low cmc condense plasmid DNA into nanometric particles and transfect cells in culture.
Dauty E; Remy JS; Blessing T; Behr JP
Laboratoire de Chimie Genetique associe CNRS/Universite Louis Pasteur de Strasbourg, Faculte de Pharmacie BP 24, 67401 Illkirch, France.
Journal of the American Chemical Society (United States) Sep 26 2001, 123 (38) p9227-34, ISSN 0002-7863 Journal Code: H59
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The size of condensed DNA particles is a key determinant for in vivo diffusion and gene delivery to cells. Gene molecules can be individually compacted by cationic thiol detergents into nanometric particles that are stabilized by oxidative conversion of the detergent into a gemini lipid. To reach the other goal, gene delivery, a series of cationic thiol detergents with various chain lengths (C(12)-C(16)) and headgroups (ornithine or spermine) was prepared, using a versatile polymer-supported synthetic strategy. Critical micelle concentrations and thiol oxidation rates of the detergents were measured. The formation and stability of complexes formed with plasmid DNA, as well as the size, xi-potential, morphology, and transfection efficiency of the particles were investigated. Using the tetradecane/ornithine detergent, a solution of 5.5 Kpb plasmid DNA molecules was converted into a homogeneous population of 35 nm particles. The same detergent, once oxidized, exhibited a typical lipid phase internal structure and was capable of effective cell transfection. The particle size did not increase with time. Surprisingly, the gel electrophoretic mobility of the DNA complexes was found to be higher than that of plasmid DNA itself. Favorable in vivo diffusion and intracellular trafficking properties may thus be expected for these complexes.

12/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11758374 21471991 PMID: 11588100
Vascular smooth muscle relaxation mediated by nitric oxide donors: a comparison with acetylcholine, nitric oxide and nitroxyl ion.
Wanstall JC; Jeffery TK; Gambino A; Lovren F; Triggle CR
School of Biomedical Sciences, Department of Physiology and Pharmacology, The University of Queensland, Brisbane, Queensland, Australia. wanstall@plpk.uq.edu.au
British journal of pharmacology (England) Oct 2001, 134 (3) p463-72, ISSN 0007-1188 Journal Code: B00
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
1. Vasorelaxant properties of three nitric oxide (NO) donor drugs

(glyceryl trinitrate, sodium nitroprusside and spermine NONOate) in mouse aorta (phenylephrine pre-contracted) were compared with those of endothelium-derived NO (generated with acetylcholine), NO free radical (NO*; NO gas solution) and nitroxyl ion (NO(-); from Angeli's salt). 2. The soluble guanylate cyclase inhibitor, ODQ (1H-(1,2,4-)oxadiazolo(4,3-a)-quinoxalin-1-one; 0.3, 1 and 10 microM), concentration-dependently inhibited responses to all agents. 10 microM ODQ abolished responses to acetylcholine and glyceryl trinitrate, almost abolished responses to sodium nitroprusside but produced parallel shifts (to a higher concentration range; no depression in maxima) in the concentration-response curves for NO gas solution, Angeli's salt and spermine NONOate. 3. The NO* scavengers, carboxy-PTIO, (2-(4-carboxyphenyl)-4,4,5,5-tetramethyl-imidazoline-1-oxyl-3-oxide; 100 microM) and hydroxocobalamin (100 microM), both inhibited responses to NO gas solution and to the three NO donor drugs, but not Angeli's salt. Hydroxocobalamin, but not carboxy-PTIO, also inhibited responses to acetylcholine. 4. The NO(-) inhibitor, L-cysteine (3 mM), inhibited responses to Angeli's salt, acetylcholine and the three NO donor drugs, but not NO gas solution. 5. The data suggest that, in mouse aorta, responses to all three NO donors involve (i) activation of soluble guanylate cyclase, but to differing degrees and (ii) generation of both NO* and NO(-). Glyceryl trinitrate and sodium nitroprusside, which generate NO following tissue bioactivation, have profiles resembling the profile of endothelium-derived NO more than that of exogenous NO. Spermine NONOate, which generates NO spontaneously outside the tissue, was the drug that most closely resembled (but was not identical to) exogenous NO.

12/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11747657 21466864 PMID: 11583173

Strain-based sequence variations and structure analysis of murine prostate specific spermine binding protein using mass spectrometry.

Chaurand P; DaGue BB; Ma S; Kasper S; Caprioli RM

Department of Biochemistry, Vanderbilt University, Nashville, Tennessee 37232-6400, USA.

Biochemistry (United States) Aug 14 2001, 40 (32) p9725-33, ISSN 0006-2960 Journal Code: A0G

Contract/Grant No.: GM 58008, GM, NIGMS

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Mouse spermine binding protein (SBP) has been characterized using mass spectrometry, including its localization within the prostate, sequence verification, and its posttranslational modifications. MALDI (matrix-assisted laser desorption/ionization) mass spectrometry was employed for localization of proteins expressed by different lobes of the mouse prostate obtained after tissue blotting on a polyethylene membrane. The mass spectra showed complex protein profiles that were different for each lobe of the prostate. The prostate-specific spermine binding protein (SBP), primarily identified by its in-source decay fragment ion signals, was found predominantly expressed by the ventral lobe of the prostate. The MALDI in-source decay measurements combined with nanoESI (nanoelectrospay ionization) MS/MS measurements obtained after specific proteolysis of SBP, allowed the exact positioning of a single N-linked carbohydrate group, and the identification of a pyroglutamate residue at the sequence N-terminus. The N-linked carbohydrate component was further investigated and the general pattern of the N-linked carbohydrate identified. The presence of a disulfide bridge between cysteine78 and cysteine124 was also established. The full sequence characterization of SBP showed several strain-based sequence differences when compared to the published gene sequence.

12/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11490638 21309940 PMID: 11404465
L-arginine-dependent suppression of apoptosis in Trypanosoma cruzi: contribution of the nitric oxide and polyamine pathways.
Piacenza L; Peluffo G; Radi R
Departamento de Bioquimica, Facultad de Medicina, Universidad de la Republica, Avenida General Flores 2125, 11800, Montevideo, Uruguay.
Proceedings of the National Academy of Sciences of the United States of America (United States) Jun 19 2001, 98 (13) p7301-6, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Until recently, a capacity for apoptosis and synthesis of nitric oxide *NO) were viewed as exclusive to multicellular organisms. The existence of these processes in unicellular parasites was recently described, with their biological significance remaining to be elucidated. We have evaluated L-arginine metabolism in Trypanosoma cruzi in the context of human serum-induced apoptotic death. Apoptosis was evidenced by the induction of DNA fragmentation and the inhibition of [3H]thymidine incorporation, which were inhibited by the caspase inhibitor Ac-Asp-Glu-Val-aspartic acid aldehyde (DEVD-CHO). In T. cruzi exposed to death stimuli, supplementation with L-arginine inhibited DNA fragmentation, restored [3H]thymidine incorporation, and augmented parasite *NO production. These effects were inhibited by the *NO synthase inhibitor N(omega)-nitroarginine methyl ester (L-NAME). Exogenous *NO limited DNA fragmentation but did not restore proliferation rates. Because L-arginine is also a substrate for arginine decarboxylase (ADC), and its product agmatine is a precursor for polyamine synthesis, we evaluated the contribution of polyamines to limiting apoptosis. Addition of agmatine, putrescine, and the polyamines spermine and spermidine to T. cruzi sustained parasite proliferation and inhibited DNA fragmentation. Also, the ADC inhibitor difluoromethylarginine inhibited L-arginine-dependent restoration of parasite replication rates, while the protection from DNA fragmentation persisted. In aggregate, these results indicate that T. cruzi epimastigotes can undergo programmed cell death that can be inhibited by L-arginine by means of (i) a *NO synthase-dependent *NO production that suppresses apoptosis and (ii) an ADC-dependent production of polyamines that support parasite proliferation.

12/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11280542 21142322 PMID: 11246218
Structure-activity analysis of the potentiation by aminothiols of the chromosome-damaging effect of bleomycin in G0 human lymphocytes.
Hoffmann GR; Buccola J; Merz MS; Littlefield LG
Department of Biology, College of the Holy Cross, Worcester, Massachusetts 01610, USA. ghoffmann@holycross.edu
Environmental and molecular mutagenesis (United States) 2001, 37 (2) p117-27, ISSN 0893-6692 Journal Code: EMM
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The radioprotective aminothiols 2-[(aminopropyl)amino] ethanethiol (WR-1065) and cysteamine (CSM) potentiate the induction of chromosomal damage by the radiomimetic compound bleomycin (BLM) in G0 human lymphocytes. To investigate the mechanism of potentiation, we measured the clastogenic activity of BLM in the cytokinesis-block micronucleus assay in the presence and absence of amines, thiols, and aminothiols. The hydroxy analog of WR-1065, 2-(3-aminopropylamino) ethanol (WR-OH), potentiates BLM

only slightly, indicating the critical nature of the thiol group. As thiols, WR-1065 and CSM may donate electrons for the activation of Fe(+2)-BLM or for the regeneration of Fe(+2)-BLM from inactive Fe(+3)-BLM. The amines putrescine, spermidine, and spermine all potentiate BLM, but they are weaker potentiators than the aminothiols, and they are effective only at high concentrations. Their activity, like that of WR-OH, is probably a consequence of conformational alteration of DNA. Dithioerythritol (DTE) and 2-mercaptoethanol (2-ME), thiols lacking an amino group, are less effective potentiators of BLM than are the aminothiols. The thiol group of WR-1065 and CSM is therefore essential, but insufficient, for explaining the strong enhancement of BLM activity. The cationic nature of CSM and WR-1065, conferred by the amino groups, evidently concentrates the active thiol function at the site of BLM action on DNA. As expected on this basis, the diamine WR-1065 is a more effective potentiator of BLM than is the monoamine CSM, whereas cysteine and N-acetylcysteine (NAC), which lack a net positive charge, potentiate BLM only weakly. These studies suggest that potentiation of the clastogenic action of BLM by aminothiols can be explained by the combination of a thiol-mediated redox mechanism and an amine-mediated targeting of the thiol function to DNA.

12/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11243958 21173709 PMID: 11259671

Role of the arginine-nitric oxide pathway in the regulation of vascular smooth muscle cell proliferation.

Ignarro LJ; Buga GM; Wei LH; Bauer PM; Wu G; del Soldato P

Department of Molecular and Medical Pharmacology, Center for the Health Sciences, University of California School of Medicine, Los Angeles, CA 90095, USA. lignarro@mednet.ucla.edu

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Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The objective of this study was to elucidate the mechanisms by which nitric oxide (NO) inhibits rat aortic smooth muscle cell (RASMC) proliferation. Two products of the arginine-NO pathway interfere with cell growth by distinct mechanisms. N(G)-hydroxyarginine and NO appear to interfere with cell proliferation by inhibiting arginase and ornithine decarboxylase (ODC), respectively. S-nitroso-N-acetylpenicillamine, (Z)-1-[N-(2-aminoethyl)-N-(2-aminoethyl)-amino]-diazen-1-ium-1,2-diolate, and a nitroaspirin derivative (NCX 4016), each of which is a NO donor agent, inhibited RASMC growth at concentrations of 1-3 microM by cGMP-independent mechanisms. The cytostatic action of the NO donor agents as well as alpha-difluoromethylornithine (DFMO), a known ODC inhibitor, was prevented by addition of putrescine but not ornithine. These observations suggested that NO, like DFMO, may directly inhibit ODC. Experiments with purified, recombinant mammalian ODC revealed that NO inhibits ODC possibly by S-nitrosylation of the active site cysteine in ODC. DFMO, as well as the NO donor agents, interfered with cellular polyamine (putrescine, spermidine, spermine) production. Conversely, increasing the expression and catalytic activity of arginase I in RASMC either by transfection of cells with the arginase I gene or by induction of arginase I mRNA with IL-4 resulted in increased urea and polyamine production as well as cell proliferation. Finally, coculture of rat aortic endothelial cells, which had been pretreated with lipopolysaccharide plus a cytokine mixture to induce NO synthase and promote NO production, caused NO-dependent inhibition of target RASMC proliferation. This study confirms the inhibitory role of the arginine-NO pathway in vascular smooth muscle

proliferation and indicates that one mechanism of action of NO is cGMP-independent and attributed to its capacity to inhibit ODC.

12/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10844832 20512513 PMID: 11056105
Nitric oxide inhibits dystrophin proteolysis by coxsackieviral protease 2A through S-nitrosylation: A protective mechanism against enteroviral cardiomyopathy.
Badorff C; Fichtlscherer B; Rhoads RE; Zeiher AM; Muelsch A; Dimmeler S; Knowlton KU
Molecular Cardiology Unit, Department of Medicine IV, Goethe-University, Frankfurt, Germany. badorff@em.uni-frankfurt.de
Circulation (UNITED STATES) Oct 31 2000, 102 (18) p2276-81, ISSN 1524-4539 Journal Code: DCV
Contract/Grant No.: GM-20818, GM, NIGMS; RO1-HL-57365-01, HL, NHLBI
Comment in Circulation. 2000 Oct 31;102(18) 2162-4; Comment in/MedlineID 20512493
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Infection with enteroviruses like coxsackievirus B3 (CVB3) as well as genetic dystrophin deficiency can cause dilated cardiomyopathy. We recently identified cleavage and functional impairment of dystrophin by the viral protease 2A during CVB3-infection as a molecular mechanism that may contribute to the pathogenesis of enterovirus-induced cardiomyopathy. Nitric oxide (NO) is elevated in human dilated cardiomyopathy, but the relevance of this finding is unknown. In mice, NO inhibits CVB3 myocarditis. Therefore, we investigated the effects of NO on the coxsackieviral protease 2A. METHODS AND RESULTS: In vitro, NO donors like PAPA-NONOate inhibited the cleavage of human and mouse dystrophin by recombinant coxsackievirus B protease 2A in a dose-dependent manner (IC(50), 51 micromol/L). In CVB3-infected HeLa cells, addition of the NO donor SNAP inhibited protease 2A catalytic activity on dystrophin. Because this inhibitory effect was reversed by the thiol-protecting agent DTT, we investigated whether NO S:-nitrosylates the protease 2A. In vitro, NO nitrosylated the active-site cysteine (C110) of the coxsackieviral protease 2A, as demonstrated by site-directed mutagenesis. Within living COS-7 cells, SNAP-induced S:-nitrosylation of this site was confirmed with electron spin resonance spectroscopy. CONCLUSIONS: These data demonstrate inactivation of a coxsackieviral protease 2A by NO through active-cysteine S:-nitrosylation in vitro and intracellularly. Given that the enteroviral protease 2A cleaves mouse and human dystrophin, NO may be protective in human heart failure with an underlying enteroviral pathogenesis through inhibition of dystrophin proteolysis.

12/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10844125 20501199 PMID: 11046123
Inhibition of endothelial cell activation by nitric oxide donors.
Zampolli A; Basta G; Lazzerini G; Feelisch M; De Caterina R
Consiglio Nazionale delle Ricerche Institute of Clinical Physiology Laboratory for Thrombosis and Vascular Research, Pisa, Italy.
Journal of pharmacology and experimental therapeutics (UNITED STATES) Nov 2000, 295 (2) p818-23, ISSN 0022-3565 Journal Code: JP3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Because nitric oxide (NO) inhibits the expression of endothelial leukocyte adhesion molecules, NO-generating compounds have major

therapeutic potential for use outside their classical indications. We report on the in vitro potential antiatherogenicity of two novel cysteine -containing NO donors, SP/W 3672, a fast spontaneous NO releaser, and its prodrug SP/W 5186, which liberates NO after bioactivation. The ability of these two compounds to inhibit monocyte adhesion and surface expression of endothelial adhesion molecules was evaluated and compared with that of other NO donors. SP/W 5186 and SP/W 3672 inhibited the adhesion of U937 monocytes to cultured human endothelial cells more potently than S-nitrosoglutathione (GSNO) or spermine NONOate, whereas nitroglycerin and isosorbide dinitrate were ineffective at comparable concentrations. A similar rank order of potency was found for the inhibition of expression of the adhesion molecules vascular cell adhesion molecule-1, intercellular adhesion molecule-1, and E-selectin as well as for major histocompatibility complex class II antigen expression. Estimated IC(50) values for vascular cell adhesion molecule-1 were >400 microM for SP/W 4744 (control for SP/W 3672 lacking the cysteine moiety), 200 microM for GSNO and spermine NONOate, 80 microM for SP/W 3672, and 50 microM for SP/W 5186. Moreover, SP/W 5186 inhibited VCAM-1 mRNA levels more potently than GSNO. This effect was likely to be transcriptional because mRNA degradation was not affected. In conclusion, SP/W 3672 and SP/W 5186 are novel potent inhibitors of endothelial activation, and this effect appears to relate to their ability to liberate NO for prolonged periods of time, either spontaneously or after conversion to active hydrolytic products.

12/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10723774 20402350 PMID: 10942576

Spermine oxidation leads to necrosis with plasma membrane phosphatidylserine redistribution in mouse leukemia cells.

Bonneau MJ; Poulin R

Laboratory of Oncology and Molecular Endocrinology, Department of Anatomy and Physiology, CHUQ Research Center, CHUL Building, 2705 Laurier Boulevard, Ste. Foy, Quebec, G1V 4G2, Canada.

Experimental cell research (UNITED STATES) Aug 25 2000, 259 (1) p23-34, ISSN 0014-4827 Journal Code: EPB

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Oxidation by copper/quinone-containing serum amine oxidases (SAO) is a well-known cause of polyamine cytotoxicity. Spermine oxidation exerts potent immunosuppressive effects in animal cells, but the cell death mechanism involved remains unclear. We compared biochemical and morphological parameters of SAO-mediated cell death in L1210 mouse leukemia cells with normal or amplified ornithine decarboxylase gene expression with those observed during apoptosis induced by deregulated polyamine uptake or by okadaic acid. None of the characteristic features of apoptotic cell death (e.g., chromatin condensation, nuclear fragmentation, internucleosomal DNA cleavage, poly(ADP-ribose) polymerase cleavage) were observed during spermine oxidation-mediated cell death, which was clearly necrotic by morphological criteria. Inhibition of a wide spectrum of caspases did not prevent SAO-dependent cell death, whereas N-acetylcysteine completely abolished the cytotoxic effects of spermine oxidation. Catalase only delayed spermine oxidation-induced cell death without affecting its modality or preventing depletion of intracellular glutathione, suggesting that both H(2)O(2) and aminoaldehydes generated by SAO-mediated spermine oxidation contribute to SAO-induced necrosis. Interestingly, redistribution of phosphatidylserine to the outer leaflet of the plasma membrane, usually a diagnostic feature of apoptosis, preceded necrotic cytolysis triggered by spermine oxidation. Thus, L1210 cell death caused by SAO-mediated spermine oxidation has all the attributes of primary necrosis, but is

also accompanied by loss of phospholipid asymmetry, indicating that the latter phenomenon may not be unique to apoptosis. Phosphatidylserine exposure, a potent engulfment signal for phagocytes, might contribute to the immunosuppressive effects of plasma polyamines through a controlled and rapid necrotic process involving SAO. Copyright 2000 Academic Press.

12/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10339354 99343009 PMID: 10416620
Differential reconstitution of mitochondrial respiratory chain activity and plasma redox state by cysteine and ornithine in a model of cancer cachexia.
Ushmorov A; Hack V; Droge W
Deutsches Krebsforschungszentrum, Division of Immunochemistry, Heidelberg, Germany.
Cancer research (UNITED STATES) Jul 15 1999, 59 (14) p3527-34, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The mechanism of wasting, as it occurs in malignant diseases and various etiologically unrelated conditions, is still poorly understood. We have, therefore, studied putative cause/effect relationships in a murine model of cancer cachexia, C57BL/6 mice bearing the fibrosarcoma MCA-105. The plasma of these mice showed decreased albumin and increased glutamate levels, which are typically found in practically all catabolic conditions. Skeletal muscles from tumor-bearing mice were found to have an abnormally low mitochondrial respiratory chain activity (mito.RCA) and significantly decreased glutathione (GSH) levels. The decrease in mito.RCA was correlated with an increase in the i.m. GSH disulfide/GSH ratio, the plasma cystine/thiol ratio, and the GSH disulfide/GSH ratio in the bile. This is indicative of a generalized shift in the redox state extending through different body fluids. Treatment of tumor-bearing mice with ornithine, a precursor of the radical scavenger spermine , reversed both the decrease in mito.RCA and the change in the redox state, whereas treatment with cysteine , a GSH precursor, normalized only the redox state. Treatment of normal mice with difluoromethyl-ornithine, a specific inhibitor of ornithine decarboxylase and spermine biosynthesis, inhibited the mito.RCA in the skeletal muscle tissue, thus illustrating the importance of the putrescine/spermine pathway in the maintenance of mito.RCA. Ornithine, cysteine, and N-acetyl-cysteine (NAC) also reconstituted the abnormally low concentrations of the GSH precursor glutamate in the skeletal muscle tissue of tumor-bearing mice. Higher doses, however, enhanced tumor growth and increased the plasma glucose level in normal mice. In the latter, cysteine and NAC also decreased i.m. catalase and GSH peroxidase activities. Taken together, our studies on the effects of ornithine, cysteine, and NAC illuminate some of the mechanistic pathways involved in cachexia and suggest targets for therapeutic intervention.

12/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10307036 98308098 PMID: 9642108
Glutathione levels determine apoptosis in macrophages.
Boggs SE; McCormick TS; Lapetina EG
Molecular Cardiovascular Research Center, Case Western Reserve University School of Medicine and University Hospitals of Cleveland, Cleveland, Ohio, 44106-4958, USA.
Biochemical and biophysical research communications (UNITED STATES) Jun 18 1998, 247 (2) p229-33, ISSN 0006-291X Journal Code: 9Y8

Contract/Grant No.: 5T32 DK07319, DK, NIDDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Spermine NONOate (SpNO, a nitric oxide donor) induced apoptosis and caspase-3 activity in the macrophage cell line RAW 267.4. RES cells that have been derived from RAW 267.4 cells by repeated exposure to lipopolysaccharide and interferon-gamma (LPS/INF-gamma), followed by outgrowth of viable cells, are resistant to apoptosis and caspase-3 activation upon exposure to SpNO. In this study we have determined that RES cells have lower levels of glutathione (GSH) and a higher oxidative state than RAW cells. Subsequently, RAW and RES cells were depleted of GSH by using l-buthionine-[S,R]-sulfoximine (BSO), a specific inhibitor of GSH synthesis. GSH depleted cells did not undergo apoptosis nor demonstrate caspase-3 activity when they were exposed to SpNO. These results suggest that the redox status of the cell is one of the key factors mediating the apoptotic pathway in which glutathione plays a critical role in mediating apoptosis via NO* and reactive oxygen species (ROS). Copyright 1998 Academic Press.

12/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10300246 98191339 PMID: 9521698
Regulation of N-arginine dibasic convertase activity by amines: putative role of a novel acidic domain as an amine binding site.
Csuhai E; Chen G; Hersh LB
Department of Biochemistry, College of Medicine, University of Kentucky, Lexington 40536-0084, USA.
Biochemistry (UNITED STATES) Mar 17 1998, 37 (11) p3787-94, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: DA02243, DA, NIDA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Peptide sequence analysis and cDNA cloning indicate that a previously described mouse arginine-specific dibasic cleaving enzyme (dynorphin converting enzyme) [Csuhai et al. (1995) Biochemistry 34, 12411] is the homologue of N-arginine dibasic convertase (NRDc) isolated from rat testis [Chesneau et al. (1994) J. Biol. Chem. 269, 2056]. A mouse NRDc cDNA exhibited 98% amino acid identity with the rat cDNA. However, within a 74 residue acidic stretch, this identity drops to 82%. Likewise, the corresponding acidic stretch of human NRDc is only 73% identical with that of rat NRDc. To reconcile previously observed kinetic differences between rat and mouse NRDc, the hydrolysis of peptide substrates by the rat, human, and mouse enzymes was compared using phosphate and Tris as buffers. Although the three NRDc's behaved similarly, Tris had a pronounced effect on the kinetics of peptide hydrolysis. With BAM-8, alpha-neoendorphin, and dynorphin B as substrates, Tris increased KM up to 40-fold with little change in Vmax, while with dynorphin A or somatostatin 28 as substrate, Tris caused a decrease in KM of up to 100 fold, again with only a modest change in Vmax. Other amines, including the polyamines putrescine, spermidine, and spermine, all affected NRD convertase activity. It is proposed that amines bind to the acidic stretch found in NRDc, and that quantitative differences in the sensitivity to amines between the rat, mouse, and human enzymes can be at least partially accounted for by differences in their acidic stretch. The role of polyamines as physiological modulators of N-arginine dibasic convertase is considered.

12/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10297421 98118237 PMID: 9457054
U937 apoptotic cell death by nitric oxide: Bcl-2 downregulation and caspase activation.
Brockhaus F; Brune B
Faculty of Medicine, Department of Medicine IV-Experimental Division, University of Erlangen-Nurnberg, Germany.
Experimental cell research (UNITED STATES) Jan 10 1998, 238 (1) p33-41, ISSN 0014-4827 Journal Code: EPB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Upon treatment with NO-releasing compounds such as S-nitrosoglutathione or spermine NO, human myeloid leukemia U937 cells undergo apoptosis. Early NO-mediated signals comprise activation of a Z-A-DCB (benzoyloxycarbonyl-Asp-CH2OC(O)-2,6-dichlorobenzene)-sensit ive, caspase-3 like cysteine protease that cleaved poly (ADP-ribose) polymerase (PARP), U1 small nuclear ribonucleoprotein (U1 snRNP), and the fluorogenic substrate N-acetyl-Asp-Glu-Val-Asp-7-amido-4-methylcoumarin. In association with these early apoptotic alterations p21 (WAF1/Cip1) is upregulated, but NO affected cell proliferation and apoptosis at a similar dose. At later time points the classical antiapoptotic protein Bcl-2 is downregulated, indicating that decreased Bcl-2 expression is secondary and not a prerequisite for initiation of apoptosis. N-Acetylcysteine (1 mM) interfered with NO-mediated apoptotic signaling, blocking DNA fragmentation as well as PARP and U1 snRNP cleavage. In contrast Z-A-DCB suppressed DNA fragmentation and U1 snRNP cleavage, while PARP breakdown proceeded unaltered. Observing proteolytic PARP digestion without apoptotic alterations questions PARP cleavage as an apoptotic parameter. These results suggest that a Z-A-DCB-sensitive caspase that is distinct from the PARP-cleaving enzyme is activated during NO exposure. NO-mediated apoptotic signaling in U937 cells activates caspases, some of which are dispensable for propagating the death signal.

12/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10293038 97445991 PMID: 9299518
Inhibition of caspase-3 by S-nitrosation and oxidation caused by nitric oxide.
Mohr S; Zech B; Lapetina EG; Brune B
Department of Medicine IV-Experimental Division, University of Erlangen Nurnberg, Loschgestrasse 8, Erlangen, 91054, Germany.
Biochemical and biophysical research communications (UNITED STATES) Sep 18 1997, 238 (2) p387-91, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Apoptotic signaling cascades converge in the activation of caspases (interleukin-1beta converting enzyme like proteases). Treatment of the human promyelocytic leukaemia cell line U937 with actinomycin D resulted in the activation of caspase-3 also known as CPP32. Protease activity was measured in cytosolic extracts by fluorometric analysis of the time-dependent cleavage of acetyl-Asp-Glu-Val-Asp-aminomethylcoumarin (DEVD-AMC), a caspase-3 substrate. Caspase activity was inhibited by thiol modifying agents such as N-ethylmaleimide or iodoacetamide and NO donors such as S-nitrosoglutathione (GSNO), BF4NO, and spermine -NO. NO-mediated enzyme inhibition was fully reversible upon the addition of DTT (dithiothreitol). NO itself was not primarily responsible for downregulation of caspase-3, as we found no correlation between rates of NO* release and the magnitude of enzyme inhibition. It is likely that S-nitrosation accounts for enzyme inhibition by various NO donors. SIN-1 and peroxynitrite were inhibitory as well. In this case, however, enzyme activity was not restored upon DTT addition, suggesting oxidation as an

additional thiol modification mechanism. Our studies provide evidence that caspases are targeted by NO via S-nitrosation and oxidation of critical thiol groups. Copyright 1997 Academic Press.

12/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10290878 97393683 PMID: 9250120
Effects of garlic thioallyl derivatives on growth, glutathione concentration, and polyamine formation of human prostate carcinoma cells in culture.
Pinto JT; Qiao C; Xing J; Rivlin RS; Protomastro ML; Weissler ML; Tao Y; Thaler H; Heston WD
Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA. pintoj@mskcc.org
American journal of clinical nutrition (UNITED STATES) Aug 1997, 66 (2) p398-405, ISSN 0002-9165 Journal Code: 3EY
Contract/Grant No.: CA 29502, CA, NCI; CA 39203, CA, NCI; DK/CA 47650, DK, NIDDK
Comment in Am J Clin Nutr. 1997 Aug;66(2) 425-6
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
This study investigated whether naturally occurring garlic derivatives and synthetic S-cysteinyl compounds that resemble garlic constituents have antiproliferative effects on human prostate carcinoma (LNCaP) cells. Studies also examined whether S-allylmercaptocysteine and S-allylcysteine affect two important molecular targets, namely reduced glutathione and polyamines. Results showed that S-allylmercaptocysteine (50 mg/L) diminished LNCaP cell growth whereas the antiproliferative effect of S-allylcysteine was not as pronounced. Studies using synthetic S-cysteinyl analogues revealed that growth inhibition was most effective with compounds containing a disulfide or an active diallyl moiety. Marginal to no inhibitory effect was observed with monosulfinic analogues. Both S-allylmercaptocysteine and S-allylcysteine caused an increase in LNCaP cell reduced glutathione concentrations. Putrescine and spermine concentrations decreased and spermidine increased 3 d after S-allylmercaptocysteine treatment. At 5 d after S-allylmercaptocysteine treatment, polyamine concentrations were similar to those of saline-treated controls. Diminished cell growth and altered polyamine concentrations suggest that S-allylmercaptocysteine may impede the polyamine synthesizing enzyme, ornithine decarboxylase, either by enhancing the formation of reduced glutathione, a known inhibitor of ornithine decarboxylase, or by reacting directly with ornithine decarboxylase at its nucleophilic thiol moiety. Because S-allylcysteine also increases reduced glutathione formation but does not significantly inhibit growth, the latter mechanism may be more likely for this compound. These data provide further evidence that nonessential nutrients derived from garlic may modulate tumor growth. Further research is required on effects of garlic derivatives in vivo before information from the present studies can be used to assist in the development of effective nutritional strategies for preventing progression of prostate cancer.

12/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10226187 99343085 PMID: 10416696
Supraphysiologic concentrations of cerulein induce apoptosis in the rat pancreatic acinar cell line AR4-2J.
Sata N; Klonowski-Stumpe H; Han B; Luthen R; Haussinger D; Niederau C
Department of Medicine, Heinrich-Heine-University of Dusseldorf, Germany.
Pancreas (UNITED STATES) Jul 1999, 19 (1) p76-82, ISSN 0885-3177

Journal Code: PRS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Little is known as yet about the role of apoptosis in pancreatic damage. This study evaluated the effects of supraphysiologic concentrations of the cholecystokinin (CCK) analog, cerulein, which causes cell damage in vitro and acute pancreatitis in vivo, on cell proliferation and DNA fragmentation in the rat pancreatic acinar cell line AR4-2J. Cerulein inhibited the cell proliferation of AR4-2J time- and dose-dependently to approximately 60% of the control level at 10(-6) M after 72 h. DNA fragmentation, as assessed by both electrophoresis and enzyme-linked immunosorbent assay (ELISA), occurred at cerulein concentrations > or = 10(-8) M. The maximal DNA fragmentation as measured by ELISA was reached after 24 h. Cerulein at concentrations > or = 10(-9) M induced wild-type p53. Glutathione (1 mM) diminished the effects of cerulein on both cell proliferation and DNA fragmentation, whereas spermine (100 microM), which partially attenuated DNA fragmentation, did not have an effect on cell proliferation. The CCK-A-receptor antagonist loxiglumide completely abolished the effect of cerulein on DNA fragmentation. The serine-protease inhibitor FUT-175 (10 microM), the cysteine-protease inhibitor NCO-700 (5 mM), and ethylene glycol tetraacetic acid (EGTA; 500 microM) all had no effects on the changes in cell proliferation and DNA fragmentation induced by cerulein. The data suggest that supraphysiologic concentrations of cerulein rapidly induce apoptosis in AR4-2J cells and only later inhibit cell proliferation. These effects are mediated by CCK-A receptors. Cerulein-induced apoptosis may involve the induction of wild-type p53 or glutathione depletion or both.

12/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10214843 99326169 PMID: 10395951

Nitric oxide can function as either a killer molecule or an antiapoptotic effector in cardiomyocytes.

Stefanelli C; Pignatti C; Tantini B; Stanic I; Bonavita F; Muscari C; Guarnieri C; Clo C; Caldarera CM

Department of Biochemistry 'G. Moruzzi', University of Bologna, Via Irnerio, 48, 40126, Bologna, Italy. cstefan@biocfarm.unibo.it

Biochimica et biophysica acta (NETHERLANDS) Jul 8 1999, 1450 (3) p406-13, ISSN 0006-3002 Journal Code: A0W

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Caspase enzymes are a family of cysteine proteases that play a central role in apoptosis. Recently, it has been demonstrated that caspases can be S-nitrosylated and inhibited by nitric oxide (NO). The present report shows that in chick embryo heart cells (CEHC), NO donor molecules such as S-nitroso-N-acetylpenicillamine (SNAP), S-nitrosoglutathione, spermine -NO or sodium nitroprusside inhibit caspase activity in both basal and staurosporine-treated cells. However, the inhibitory effect of NO donors on caspase activity is accompanied by a parallel cytotoxic effect, that precludes NO to exert its antiapoptotic capability. N-Acetylcysteine (NAC) at a concentration of 10 mM blocks depletion of cellular glutathione and cell death in SNAP-treated CEHC, but it poorly affects the ability of SNAP to inhibit caspase activity. Consequently, in the presence of NAC, SNAP attenuates not only caspase activity but also cell death of staurosporine-treated CEHC. These data show that changes in the redox environment may inhibit NO-mediated toxicity, without affecting the antiapoptotic capability of NO, mediated by inhibition of caspase enzymes. NO may thus be transformed from a killer molecule into an antiapoptotic agent.

12/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10091977 99160369 PMID: 10049493
Zinc as an inducer of the membrane permeability transition in rat liver mitochondria.
Wudarczyk J; Debska G; Lenartowicz E
Nencki Institute of Experimental Biology, Pasteur 3, Warsaw, Poland.
Archives of biochemistry and biophysics (UNITED STATES) Mar 1 1999, 363 (1) p1-8, ISSN 0003-9861 Journal Code: 6SK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
It is shown that 2-10 microM Zn2+ induces swelling of rat liver mitochondria incubated in a buffered sucrose medium either with valinomycin or with FCCP, Ca2+, ionophore A23187, oligomycin, and nigericin. This swelling was associated with the release of GSH from mitochondria. Both processes were sensitive to known inhibitors of the mitochondrial permeability transition (MPT), cyclosporin A, and Mg2+. Mitochondrial swelling induced by Zn2+ was also inhibited by rotenone, antymycin A, N-ethylmaleimide, butylhydroxytoluene, and spermine, whereas it was stimulated by tert-butyl hydroperoxide, diamide, and monobromobimane. It did not require the addition of phosphate. The same sensitivity to pH of the mitochondrial swelling induced by Zn2+ and by phenylarsine oxide suggests the same site of the interaction, namely, thiol groups. The ability of Zn2+ to induce mitochondrial swelling gradually decreased along with its increasing concentration above 10 microM. It is concluded that micromolar Zn2+ induces the MPT presumably by the interaction with cysteinyl residues. This process is independent of the mitochondrial membrane potential. Copyright 1999 Academic Press.

12/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10064050 98296139 PMID: 9630648
Inhibitors of interleukin-1 beta-converting enzyme-family proteases (caspases) prevent apoptosis without affecting decreased cellular ability to reduce 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide in cerebellar granule neurons.
Harada J; Sugimoto M
Neuroscience Research Laboratories, Sankyo, 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan. jyunha@shina.sankyo.co.jp
Brain research (NETHERLANDS) May 18 1998, 793 (1-2) p231-43, ISSN 0006-8993 Journal Code: B5L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We assessed the possible role of interleukin-1beta-converting enzyme-family proteases (caspases) in apoptosis in cultured rat cerebellar granule neurons. CPP32 (caspase-3)-like protease activity was augmented by low KCl treatment, preceding neuronal cell death. Agents such as brain-derived neurotrophic factor (BDNF), dibutylyl cAMP, NMDA, actinomycin D, S-adenosyl-L-methionine, and spermine prevented apoptosis. For various neuroprotective agents, the degree of apoptosis prevention correlated with the prevention of the activation of CPP32-like protease. Furthermore, Z-Asp-2, 6-dichlorobenzoyloxy-methylketone (Z-Asp-CH2-DCB), Boc-Asp-fluoromethylketone (Boc-Asp-FMK), and Z-Val-Ala-Asp-fluoromethylketone (Z-VAD-FMK), which are inhibitors of caspases, also prevented apoptosis. In contrast to many other neuroprotective agents, these inhibitors of caspases showed little effect on the decrease of cellular 3-[4,5-dimethylthiazol-2-yl]-2, 5-diphenyltetrazolium bromide (MTT) reduction activity after low KCl treatment. The neurons rescued by these

inhibitors of caspases during low KCl treatment were in a hypoenergic state in their ATP levels and vulnerable to subsequent treatment with medium containing high KCl or glutamate which induce an influx of Ca2+, but which are less toxic to normal neurons. These results suggest that caspase(s) are involved in the apoptosis of cerebellar granule neurons and that several agents protect neurons from death by blocking the activation of the protease(s). Although several caspase inhibitors examined in this study protect neurons from apoptosis, rescued neurons are vulnerable to subsequent stimuli that induce necrotic cell death. Copyright 1998 Elsevier Science B.V.

12/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09853575 98381066 PMID: 9705871
Inhibition of clotting factor XIII activity by nitric oxide.
Catani MV; Bernassola F; Rossi A; Melino G
IDI-IRCCS, Biochemistry Laboratory, Department of Experimental Medicine, University of Rome Tor Vergata, Italy.
Biochemical and biophysical research communications (UNITED STATES) Aug 10 1998, 249 (1) p275-8, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The plasma factor XIII (FXIII) is a transglutaminase which catalyzes the cross-linking of fibrin monomers during blood coagulation. S-nitrosylation of protein sulfhydryl groups has been shown to regulate protein function. Therefore, to establish whether nitric oxide (NO) affects the enzymatic activity of FXIII, we studied the effect of the NO-donor S-nitroso-N-acetylpenicillamine (SNAP) in a blood coagulation test in vitro. High concentrations of SNAP were found to have inhibitory effects on clot formation. Moreover, specific formation of gamma-dimers through the action of FXIII is selectively inhibited by high concentrations of SNAP, as revealed by Western blot. Purified activated FXIII and plasma preparations were then exposed to NO-donor compounds and the enzyme activity was assayed by measuring the incorporation of [3H] putrescine into dimethylcasein. The NO donors, SNAP, spermine-NO (SPER-NO) and 3-morpholinosydnonimine (SIN-1), and the NO-carrier, S-nitrosoglutathione (GSNO), inhibited FXIII activity in a dose-dependent manner, in both purified enzyme and plasma preparations. Titration of -SH groups of FXIII with [14C] iodoacetamide has shown that the number of titratable cysteines per monomer of FXIII decreased from 1 (in absence of NO donors) to 0 (in the presence of NO donors). These results demonstrate that blood coagulation FXIII is a target for NO both in vitro and in vivo, and that inhibition occurs by S-nitrosylation of a highly reactive cysteine residue. In conclusion, we show that inhibition of FXIII activity by NO may represent an additional regulatory mechanism for the formation of blood clot with physio-pathological implications.

12/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09480251 98042137 PMID: 9374724
Regulation of heme oxygenase-1 gene expression in vascular smooth muscle cells by nitric oxide.
Hartsfield CL; Alam J; Cook JL; Choi AM
Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21224, USA.
American journal of physiology (UNITED STATES) Nov 1997, 273 (5 Pt 1) pL980-8, ISSN 0002-9513 Journal Code: 3U8
Contract/Grant No.: DK-43135, DK, NIDDK
Languages: ENGLISH

Document type: Journal Article
Record type: Completed

Heme oxygenase (HO)-mediated heme degradation is the primary mechanism for production of cellular carbon monoxide (CO). Analogous to nitric oxide (NO), CO mediates physiological and cellular functions such as vasodilation, stimulation of guanylate cyclase, and neuronal transmission. In view of accumulating data demonstrating a correlation between the activity of these two gaseous molecules and that the predominant source of CO is via HO catalysis, we hypothesized that NO regulates HO expression. We demonstrate that the NO donor spermine NONOate (SNN) increases steady-state levels of HO-1 mRNA in aortic vascular smooth muscle cells (aSMC) in both a time- and dose-dependent manner. The accumulation of HO-1 mRNA that correlated with increased HO-1 protein synthesis resulted from both an increased rate of gene transcription and a decreased rate of mRNA turnover. Inhibition of the NO-induced HO-1 mRNA expression by cycloheximide suggests that new protein synthesis is required for increased HO-1 gene expression. Induction of HO-1 expression by SNN occurs in a guanosine 3',5'-cyclic monophosphate (cGMP)-independent manner because exposure of cells to 8-bromoguanosine 3',5'-cyclic monophosphate, a cGMP analog, did not increase HO-1 mRNA levels, and pretreatment of cells with 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one, a selective guanylate cyclase inhibitor, did not prevent SNN-induced HO-1 mRNA accumulation. The antioxidant N-acetyl-L-cysteine markedly inhibited SNN-induced HO-1 mRNA expression, whereas peroxynitrite did not induce HO-1 expression in aSMC. Interestingly, CO did not attenuate NO-induced HO-1 expression through an autocrine negative feedback mechanism as had been observed for hypoxia-induced HO-1 expression. These data provide evidence for an important regulatory network between NO and CO via HO-1.

12/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09467653 97350805 PMID: 9207181

Endogenous ADP-ribosylation of a G(alpha i) protein in bovine ciliary body is stimulated by nitric oxide.

Pozdnyakov N; Margulis A; Sitaramayya A
Eye Research Institute, Oakland University, Rochester, Michigan 48309, USA.

Biochemical and biophysical research communications (UNITED STATES) Jun 27 1997, 235 (3) p482-6, ISSN 0006-291X Journal Code: 9Y8
Contract/Grant No.: EY 05230, EY, NEI; EY 07158, EY, NEI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Five ciliary body membrane proteins were labeled when incubated with (adenylate-32P)NAD. Nitric oxide donors stimulated the labeling of 64, 40, and 29-30 kDa proteins and inhibited that of 58 and 56 kDa proteins. The greatest influence of nitric oxide was on the 40 kDa protein: a 17-fold stimulation. Western blotting and immunoprecipitation with specific antibodies identified this protein as the alpha-subunit of G(i-1). Studies with inhibitors showed that the protein was mono-ADP-ribosylated. Treatment of (32P)NAD-labeled G(i-1) with Hg and analysis of the released radioactive material showed that the protein was ADP-ribosylated on a cysteine residue.

12/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09464531 97270327 PMID: 9125410

Polyamines prevent apoptotic cell death in cultured cerebellar granule neurons.

Harada J; Sugimoto M

Neuroscience Research Laboratories, Sankyo Co. Ltd., Shinagawa-ku, Tokyo, Japan. jyunha@shina.sankyo.co.jp

Brain research (NETHERLANDS) Apr 11 1997, 753 (2) p251-9, ISSN 0006-8993 Journal Code: B5L

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Polyamines play critical roles during the development of brain neurons. In the present study we examined the effects of polyamines on neuronal apoptotic death. Rat cerebellar granule neurons were cultured in the presence of a depolarizing concentration of KCl (25 mM) in the medium. Apoptotic neuronal death was induced by changing the medium to that containing 5.6 mM KCl without serum. Spermine as well as spermidine and putrescine prevented cell death in a concentration-dependent manner with the order of potency being spermine > spermidine > putrescine. The effect of spermine was partially blocked by several NMDA-type glutamate receptor antagonists including (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine (MK-801). MK-801-sensitive neuroprotection by spermine depended on cell density. Activation of CPP32 (caspase-3/Yama/apopain)-like proteolytic activity, a key mediator of apoptosis, precedes neuronal death, and polyamines prevented an increase in this activity. These results demonstrate that polyamines protect neurons from apoptotic cell death through both NMDA receptor-dependent and -independent mechanisms, acting upstream from the activation of CPP32-like protease(s).

12/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09220059 96262435 PMID: 8845915

Streptozotocin is not a spontaneous NO donor.

Kroncke KD; Kolb-Bachofen V

Research Group Immunobiology in the Biomedical Research Centre, Heinrich-Heine-University, Dusseldorf, FRG.

Free radical research (SWITZERLAND) Feb 1996, 24 (2) p77-80, ISSN 1071-5762 Journal Code: BW3

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The reaction of streptozotocin with oxymyoglobin was analyzed and compared with results using various compounds that spontaneously generate nitric oxide in solution.

12/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09218686 96361337 PMID: 8752308

Binding of radioprotective thiols and disulfides in Chinese hamster V79 cell nuclei.

Newton GL; Aguilera JA; Ward JF; Fahey RC

Department of Chemistry, University of California, San Diego, La Jolla 92093, USA.

Radiation research (UNITED STATES) Sep 1996, 146 (3) p298-305, ISSN 0033-7587 Journal Code: QMP

Contract/Grant No.: CA 35982, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Binding of thiols of varying charge (Z) in nuclei prepared in suspension was determined to assess the extent to which histones, Mg2+ spermine and chromatin structure influence counter-ion condensation of cationic thiols and co-ion depletion of anionic thiols at DNA. The nuclei were

prepared in suspension buffer, washed and incubated in buffer containing thiol and graded amounts of Mg2+ and spermine. The nuclei were separated from the incubation medium by centrifugation through silicone oil, and the thiols were determined in the nuclear pellet and in the incubation buffer by labeling with monobromobimane and HPLC. Measurements of the water content of nuclei indicated that chromatin was fully condensed in buffer containing 5 mM MgCl2 and 115 mM KCl. Under these conditions nuclei incubated in 1 mM substrate had concentrations of 0.80 +/- 0.21 mM glutathione (Z = -1), 1.05 +/- 0.12 mM 2-mercaptoethanol (Z = 0), 0.95 +/- 0.15 mM cysteine (Z = 0), 0.75 +/- 0.29 mM cysteamine (Z = +1), 2.5 +/- 0.3 mM WR-1065 (Z = +2), 3.4 +/- 0.5 mM WR-35980 (Z = +3) and 12 +/- 2 mM WR-33278 (disulfide of WR-1065, Z = +4), respectively. Spermine up to 1 mM in the presence of 5 mM Mg2+ had little effect upon the binding of these thiols and disulfide, but did suppress the binding of 0.1 mM WR-33278, the results indicating that WR-33278 and spermine compete for the same sites with comparable affinity. From the results observed and the assumption that deviations from the bulk solution concentration (1 mM) result from counter-ion condensation within 3 nm of DNA, we estimate that WR-1065 (Z = +2), WR-35980 (Z = +3) and WR-33278 (Z = +4) were concentrated near DNA 6-, 8- and 20-fold, respectively, in the presence of histones, 5 mM Mg2+ and 1.0 mM spermine.

12/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09185665 96285078 PMID: 8691603
[Amines and pteridines]
Shimpo K; Chihara T; Hibiya M; Ito S; Nagatsu T
Institute for Comprehensive Medical Science, School of Medicine, Fujita Health University.
Nippon rinsho (JAPAN) Jun 1996, 54 (6) p1515-20, ISSN 0047-1852 Journal Code: KIM
Languages: JAPANESE
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Polyamines (putrescine, spermidine and spermine) play important roles in cell proliferation and differentiation, and have been established as tumors markers. We and other workers have confirmed that N1-acetylspermidine in tumor tissues, spermidine and spermine in erythrocytes, and N1,N12-diacetylspermine in urine might be the most sensitive indicators for various forms of tumors. Neopterin is a marker of cell-mediated immunostimulation, and may be a helpful marker in monitoring cancer patients. HPLC and immunological assays of neopterin, biopterin, and N2-(3-aminopropyl)biopterin(oncopterin) in urine might be useful in the clinical study of pteridines, as cancer markers. Serum 5-S-cysteinyldopa level is a useful and specific biochemical marker for malignant melanoma.

12/3,AB/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08979309 96341123 PMID: 8729005
Counter modulation of adipocyte mitochondrial processes by insulin and S-oxalylglutathione.
Moore KH; Tsatsos P; Staudacher DM; Kiechle FL
Department of Chemistry, Oakland University, Rochester, MI 48309-4401, USA.
international journal of biochemistry & cell biology (ENGLAND) Feb 1996, 28 (2) p183-91, ISSN 1357-2725 Journal Code: CDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Oxalyl thiolesters, a group of putative intracellular regulators, have been shown to be in vitro inhibitors of some cytosolic enzymes which are stimulated by insulin. In this study, the effects of insulin and oxalyl thiolesters on pyruvate dehydrogenase, beta-oxidation, and acyl-CoA hydrolase activities in mitochondria from rat epididymal adipocytes are compared. Using glutathione, CoASH, cysteine, and cysteamine as thiol sources, oxalyl thioesters were synthesized, purified, and quantitated. Mitochondria were isolated from rat epididymal adipocytes, some of which were incubated with or without insulin. Mitochondrial activities were determined by radioisotopic assay subsequent to control, insulin, or oxalyl thiolester incubation. Under the conditions used in this study, pyruvate dehydrogenase activity was increased 28% subsequent to 10-min incubation of adipocytes with 400 microU/ml insulin; in contrast, preincubation of adipocyte mitochondria with S-oxalylglutathione resulted in a dose-dependent 11-19% inhibition of pyruvate dehydrogenase. S-oxalylglutathione also attenuated the spermine-induced activation of pyruvate dehydrogenase. Insulin treatment resulted in a small but significant increase in beta-oxidation of palmitic acid while 100 microM S-oxalylglutathione mediated a 40% decrease in palmitate oxidation. Palmitoyl-CoA hydrolase activity was decreased 14% by insulin treatment; however, S-oxalylglutathione caused a 14-50% increase in hydrolase activity. The other oxalyl thiolesters were not as effective or as consistent as S-oxalylglutathione in modulation of the mitochondrial activities; free thiols and oxalic acid did not modulate the activities. In summary, pyruvate dehydrogenase, palmitate beta-oxidation, and palmitoyl-CoA hydrolase activities in adipocyte mitochondria were modulated in approximately equal but opposite directions by insulin and S-oxalylglutathione. These findings support the suggestion that oxalyl thiolesters may function as an intracellular signal recruited to return insulin to normal levels.

12/3,AB/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08907597 96008062 PMID: 8567475

Toxicity and growth-promoting potential of spermine when fed to chicks.

Sousadias MG; Smith TK
Department of Nutritional Sciences, University of Guelph, Ontario, Canada.

Journal of animal science (UNITED STATES) Aug 1995, 73 (8) p2375-81, ISSN 0021-8812 Journal Code: HC7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Previous studies have shown that the feeding of putrescine, a biogenic amine and the precursor of the mammalian polyamines, can promote whole-body growth of chicks. The current study was undertaken to determine the effect of spermine , also a biogenic amine and the most cationic of the polyamines, under similar conditions. In Exp. 1, 120 week-old chicks were fed purified crystalline amino acid-based diets containing 0, .2, .4, .6, .8, or 1.0% spermine for 14 d. Spermine proved highly toxic and growth rates were reduced compared with controls when even .2% was fed. In Exp. 2, chicks were fed 0, .0375, .0750, or .1000% spermine. These concentrations proved less toxic than those used in Exp. 1. Supplemental dietary cysteine was then provided at 0, .3, .6, and .9% together with 0, .025, .050, or .400% spermine (Exp. 3) because depletion of cellular glutathione has been suggested as contributing to spermine's toxicity. Even high levels of cysteine supplementation did not overcome spermine 's toxicity. Subsequent dietary provision of L-2-oxothiazolidine-4-carboxylic acid (OTC, Exp. 4), a cysteine prodrug, showed that depletion of cellular glutathione was not likely a cause of spermine toxicosis. A trend toward increased weight gain and

feed efficiency was observed when low concentrations of spermine were fed. It was concluded, however, that dietary spermine was more toxic to chicks than was previously seen for putrescine, that any growth-promoting effects of dietary spermine are small, and that supplements of dietary cysteine or OTC are unlikely to increase these effects by overcoming spermine toxicosis.

12/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08884311 95033214 PMID: 7524561
Identification of two cysteine residues that are required for redox modulation of the NMDA subtype of glutamate receptor.
Sullivan JM; Traynelis SF; Chen HS; Escobar W; Heinemann SF; Lipton SA
Molecular Neurobiology Laboratory, Salk Institute, La Jolla, California 92037.
Neuron (UNITED STATES) Oct 1994, 13 (4) p929-36, ISSN 0896-6273 Journal Code: AN8
Contract/Grant No.: EY05477, EY, NEI; HD29587, HD, NICHD; MH10270, MH, NIMH; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Modulation of NMDA-mediated responses by oxidizing and reducing reagents has been described in a variety of neuronal preparations. Here, we report that NMDA-gated currents of oocytes expressing heteromeric NMDA receptors are also modulated by sulfhydryl redox reagents. Each cysteine residue in the NMDAR1 (NR1) subunit and each conserved NMDAR2 (NR2) cysteine residue in a prototypical subunit (NR2B) was tested for its role in redox modulation. We have identified 2 cysteines in the NR1 subunit that are required for redox modulation of NMDA-gated currents in oocytes expressing NR1-NR2B, NR1-NR2C, or NR1-NR2D receptors. Mutation of these same 2 cysteines also eliminated potentiation by spermine and shifted the IC50 for H+ inhibition and the EC50 for NMDA. Redox modulation of heteromeric NR1-NR2A receptors appeared to be different from that of the other heteromeric receptors, indicating the presence of one or more unique redox modulatory sites on NR1-NR2A receptors.

12/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08687348 96010324 PMID: 8538190
Ornithine decarboxylase as a target for chemoprevention.
Pegg AE; Shantz LM; Coleman CS
Department of Cellular and Molecular Physiology, Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, Hershey 17033, USA.
Journal of cellular biochemistry (UNITED STATES) 1995, 22 p132-8, ISSN 0733-1959 Journal Code: K8K
Contract/Grant No.: CA-18138, CA, NCI; GM-26290, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
1-Ornithine decarboxylase (ODC) is essential for polyamine synthesis and growth in mammalian cells; it provides putrescine that is usually converted into the higher polyamines, spermidine and spermine. Many highly specific and potent inhibitors of ODC are based on the lead compound alpha-difluoromethylornithine (DFMO), which is an enzyme-activated irreversible inhibitor. DFMO is accepted as a substrate by ODC and is decarboxylated, leading to the formation of a highly reactive species that forms a covalent adduct with either cysteine-360 (90%) or lysine-69 (10%). Both modifications inactivate the enzyme. ODC activity is normally

very highly regulated at both transcriptional and post-transcriptional levels according to the growth state of the cell and the intracellular polyamine content. Experimental over-production of ODC can be caused by either transfection with plasmids containing the ODC cDNA with part of the 5'-untranslated region (5'UTR) deleted under the control of a very strong viral promoter, or transfection of plasmids that cause the overproduction of eIF-4E, reported to be a limiting factor in the translation of mRNAs with extensive secondary structures in the 5'UTR. In both cases, unregulated overexpression of ODC transforms NIH 3T3 cells to a neoplastic state. Along with studies showing that many tumor promoters increase ODC activity and that a number of preneoplastic conditions and tumor samples show high levels of ODC, these results suggest that ODC may act as an oncogene in an appropriate background. This provides a rationale for the possible use of ODC inhibitors as chemopreventive agents.(ABSTRACT TRUNCATED AT 250 WORDS)

12/3,AB/32 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07842532 92113610 PMID: 1765786
Changes in ornithine decarboxylase activity and polyamine levels in response to eight different forms of selenium.
Thompson HJ; Ip C; Ganther HE
Laboratory of Nutrition Research, AMC Cancer Research Center, Denver, Colorado 80214.
Journal of inorganic biochemistry (UNITED STATES) Dec 1991, 44 (4) p283-92, ISSN 0162-0134 Journal Code: JAR
Contract/Grant No.: CA 45614, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The biological activity of selenium is known to depend on its chemical form. In this study, eight forms of selenium that differed in oxidation state or degree of methylation were studied for their acute effects on the activities of ornithine decarboxylase (ODC) and S-adenosylmethionine decarboxylase (AdoMet DC) and on the concentrations of the polyamines putrescine, spermidine, and spermine in the liver. The polyamine pathway was studied because it is involved in the control of cell growth and in the cell's response to trophic, carcinogenic, and toxic stimuli, activities that selenium has been reported to affect. Female Sprague Dawley rats were administered 12 mumol Se/kg body weight via intraperitoneal injection and were sacrificed six hours later. Injection of sodium selenate, sodium selenite, selenomethionine, Se-methylselenocysteine, selenobetaine, and selenobetaine methyl ester resulted in significant increases in liver selenium, whereas injection of dimethylselenoxide and trimethylselenonium chloride did not. ODC activity and AdoMet DC activity were induced by those selenium compounds that also increased liver selenium content, but the magnitude of enzyme induction by those compounds was not correlated with the hepatic concentration of total selenium determined fluorometrically. Furthermore, the induction of ODC activity by the various forms of selenium did not result in concomitant increases in putrescine, spermidine, and spermine except in the case of selenite. Given that alterations in the metabolism of selenium are induced when the level of tissue selenium is elevated and that the relative abundance of various selenometabolites can be affected by the point of entry of selenium into intermediary metabolism, these data suggest that the changes that were observed in enzyme activities and polyamine levels are likely to be associated with the accumulation of a specific metabolite of selenium. The relevance of these findings to elucidation of the biological activities attributable to various forms of selenium is under investigation.

12/3,AB/33 (Item 33 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07822336 90373793 PMID: 2397214
The formation of cytochrome P-450 from cytochrome P-420 is promoted by spermine.
Hui Bon Hoa G; Di Primo C; Geze M; Douzou P; Kornblatt JA; Sligar SG
U310, INSERM, Service de Biospectroscopy, Paris, France.
Biochemistry (UNITED STATES) Jul 24 1990, 29 (29) p6810-5, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
This paper is concerned with camphor-bound bacterial cytochrome P-450 and processes that alter its spin-state equilibrium and influence its transition to the nonactive form, cytochrome P-420, as well as its renaturation to the native camphor-bound cytochrome P-450. Spermine, a polycation carrying a charge of 4 +, and potassium, a monovalent cation, were shown to differently cause an increase of high-spin content of camphor-bound cytochrome P-450. The spermine-induced spin transition saturates around 75% of the high spin; a further addition of KCl to the spermine -containing sample shifted the spin state to 95% of the high spin. The volume change of these spin transitions as measured by the use of high pressure indicated an excess of -40 mL/mol for the sample containing potassium as compared to that containing spermine. These results suggest that the proposed privileged site for potassium has not been occupied by spermine and that pressure forces both the camphor and the potassium ion from its sites, allowing solvent movement into the protein as well as ordering of solvent by the excluded camphor and potassium. Cytochrome P-420 was produced from cytochrome P-450 by hydrostatic pressure in the presence of potassium, spermine, and cysteine . Potassium cation shows a bigger effect on the stability of cytochrome P-450 than spermine or cysteine, as revealed by a higher value of the pressure of half-inactivation, P1/2, and a bigger inactivation volume change. However, potassium cation did not promote renaturation of cytochrome P-420 to cytochrome P-450 while the presence of spermine did.(ABSTRACT TRUNCATED AT 250 WORDS)

12/3,AB/34 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07821183 90335282 PMID: 2378899
Interaction of human erythrocyte multicatalytic proteinase with polycations.
Mellgren RL
Department of Pharmacology and Therapeutics, Medical College of Ohio, Toledo 43699-0008.
Biochimica et biophysica acta (NETHERLANDS) Aug 1 1990, 1040 (1) p28-34, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: HL 36573, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The multicatalytic proteinase from human erythrocytes (macropain, proteasome) is a large enzyme composed of at least six distinct subunits ranging in molecular masses from 20 to 30 kDa. As its name implies, this proteinase appears to contain multiple catalytic sites with differing specificities toward peptide substrates. Several polycationic substances, including polylysines, polyarginine, protamine and histone H1 markedly stimulated caseinolytic activity of the proteinase. Activation was instantaneous, and involved increasing the Vmax of the proteinase for casein. Prolonged preincubation with polylysine at 37 degrees C resulted in autolytic inactivation of the proteinase. The polylysine concentrations required for half-maximal activation or autolytic inactivation were the

same. A 23 kDa subunit of the proteinase disappeared at the same rate as loss of catalytic activity, and with the same pH dependence and polylysine concentration dependence. These results suggest that polylysine perturbs the structure of the multicatalytic proteinase, resulting in increased catalytic activity toward substrates; and, with prolonged exposure, allowing autoproteolytic inactivation to occur. The 23 kDa subunit appeared to be required for expression of caseinolytic activity, and may therefore be a catalytic subunit of the complex having activity against casein.

12/3,AB/35 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06030710 89197928 PMID: 2495283
The beta subunit of tryptophan synthase. Clarification of the roles of histidine 86, lysine 87, arginine 148, cysteine 170, and cysteine 230.
Miles EW; Kawasaki H; Ahmed SA; Morita H; Morita H; Nagata S
Section on Pharmacology, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland 20892.
Journal of biological chemistry (UNITED STATES) Apr 15 1989, 264 (11) p6280-7, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Our studies, which are aimed at understanding the catalytic mechanism of the beta subunit of tryptophan synthase from Salmonella typhimurium, use site-directed mutagenesis to clarify the functional roles of several putative active site residues. Although previous chemical modification studies have suggested that histidine 86, arginine 148, and cysteine 230 are essential residues in the beta subunit, our present findings that beta subunits with single amino acid replacements at these positions have partial activity show that these 3 residues are not essential for catalysis or substrate binding. These conclusions are consistent with the recently determined three-dimensional structure of the tryptophan synthase alpha 2 beta 2 complex. Amino acid substitution of lysine 87, which forms a Schiff base with pyridoxal phosphate in the wild type beta subunit, yields an inactive form of the beta subunit which binds alpha subunit, pyridoxal phosphate, and L-serine. We also report a rapid and efficient method for purifying wild type and mutant forms of the alpha 2 beta 2 complex from S. typhimurium from an improved enzyme source. The enzyme, which is produced by a multicopy plasmid encoding the trpA and trpB genes of S. typhimurium expressed in Escherichia coli, is crystallized from crude extracts by the addition of 6% poly(ethylene glycol) 8000 and 5 mM spermine. This new method is also used in the accompanying paper to purify nine alpha 2 beta 2 complexes containing mutant forms of the alpha subunit.

12/3,AB/36 (Item 36 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05782377 88198241 PMID: 2834387
Characterization of the major protein-tyrosine-phosphatases of human placenta.
Tonks NK; Diltz CD; Fischer EH
Department of Biochemistry, University of Washington, Seattle 98195.
Journal of biological chemistry (UNITED STATES) May 15 1988, 263 (14) p6731-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AM07902, AM, NIADDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In the preceding article (Tonks, N. K., Diltz, C. D., and Fischer, E. H. (1988) J. Biol. Chem. 263, 6722-6730), the purification of the major

protein-tyrosine-phosphatases from human placenta, some to apparent homogeneity, was described. This report compares the characteristics of these enzymes and clearly identifies at least two distinct protein-tyrosine-phosphatase catalytic subunits. All were absolutely specific for phosphotyrosyl residues and showed no activity on any of the phosphoseryl/phosphothreonyl-containing proteins tested; they exhibited a high affinity for substrate with Km values in the submicromolar range. All were absolutely dependent on sulfhydryl compounds and appeared to contain at least one highly reactive cysteinyl residue essential for activity. Subtypes 1A and 1B could be distinguished by their response to polyanionic and polycationic compounds. The 1B enzymes were activated by EDTA, spermine , spermidine, and myelin basic protein to a greater extent than the 1A subtypes. Furthermore, they were inhibited by approximately 2 orders of magnitude lower concentrations of heparin (IC50 approximately 20 nM) and 1:1 or 4:1 poly (glutamate/tyrosine) (IC50 approximately 50 nM) than the 1A subtypes. Surprisingly, inhibition by the glutamate/tyrosine copolymers was strictly noncompetitive. Peptide mapping following digestion with Achromobacter protease I or Staphylococcus aureus V8 protease supported the view that, whereas protein-tyrosine-phosphatase subtypes 1A and 1B are different, their soluble and particulate counterparts are closely related structurally and are distinct from serine/threonine phosphatases 1 and 2A.

12/3,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04903299 84035382 PMID: 6631547
The influence of cysteine and methionine supplements on polyamine biosynthesis in the rat.
Acuff RV; Smith JT
Journal of nutrition (UNITED STATES) Nov 1983, 113 (11) p2295-9, ISSN 0022-3166 Journal Code: JEV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Previous reports from this laboratory have shown that supplementation of diets containing the optimal level (0.02%) of dietary inorganic sulfate (SO4(2-] with cysteine instead of methionine can affect several metabolic pathways. It is possible that these results reflect alterations in the biosynthesis of potent physiological compounds, the polyamines. Adult male albino rats were fed diets containing 15% casein and a constant level of inorganic sulfate (0.02%) supplemented with cysteine (0.505%) or methionine (0.62%). The polyamines (putrescine, spermidine and spermine) and the controlling enzymes for their biosynthesis ornithine decarboxylase (ODC) and S-adenosylmethionine decarboxylase (SAMD) were evaluated in liver, kidney and brain tissue homogenates following a 17-day dietary period. Rats fed the diet supplemented with cysteine had increased ODC activity and decreased SAMD activity when compared to rats fed diets supplemented with methionine. Polyamine concentrations varied in tissues with a trend toward increasing amounts in animals fed the cysteine -supplemented diet. Based on these data, it appears that dietary cysteine stimulates the biosynthesis and increased tissue concentration of polyamines.

12/3,AB/38 (Item 38 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04086667 81110451 PMID: 6257275
Valyl-tRNA synthetase form yellow lupin seeds: hydrolysis of the enzyme-bound noncognate aminoacyl adenylate as a possible mechanism of increasing specificity of the aminoacyl-tRNA synthetase.
Jakubowski H

Biochemistry (UNITED STATES) Oct 28 1980, 19 (22) p5071-8, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

12/3,AB/39 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04074668 84065464 PMID: 6580476
Effect of polyamines on acidified ethanol-induced gastric lesions in rats.
Mizui T; Doteuchi M
Japanese journal of pharmacology (JAPAN) Oct 1983, 33 (5) p939-45, ISSN 0021-5198 Journal Code: KO7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The participation of polyamines and nonprotein sulfhydryls in the gastric cytoprotective mechanisms was studied using gastric mucosal lesions produced by acidified ethanol in rats as an experimental model. Treatment with prostaglandin E2 (PGE2), but not cimetidine, prevented the formation of gastric mucosal lesions. Oral administration of cadaverine, spermidine and spermine prevented the lesion formation by acidified ethanol in a dose-dependent manner. Indomethacin or acetazolamide had no influence on the cytoprotective effect of spermine, whereas sulfhydryl blockers such as iodoacetamide and N-ethylmaleimide partially blocked it. Sulfhydryl compounds such as cysteine, reduced glutathione (GSH), and cysteamine prevented the lesion formation induced by acidified ethanol. The concentration of nonprotein sulfhydryls in the gastric mucosa was significantly decreased at 1 hr after administration of acidified ethanol, and this decrease was partially prevented by spermine or PGE2. These results suggest that the cytoprotective effect of spermine may not be mediated by endogenous prostaglandins or alkaline secretion in the gastric mucosa, but may be partially related to endogenous sulfhydryl compounds.

12/3,AB/40 (Item 40 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03503114 77157240 PMID: 851438
Interaction between insulin receptors and glucose transport: effect of prostaglandin E2.
Olefsky JM
Biochemical and biophysical research communications (UNITED STATES) Mar 21 1977, 75 (2) p271-6, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

12/3,AB/41 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03164475 79192763 PMID: 447201
Comparison of the effects of insulin and insulin-like agents on different aspects of adipocyte metabolism.
Olefsky JM
Hormone and metabolic research (GERMANY, WEST) Mar 1979, 11 (3) p209-13, ISSN 0018-5043 Journal Code: GBD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The effect of insulin, spermine, cysteine, and diamide on glucose transport, glucose oxidation, and lipolysis were compared using isolated rat adipocytes. Each agent exerted insulin-like effects on glucose transport and glucose oxidation, whereas spermine and cysteine, but not diamide, inhibited lipolysis. Furthermore, the relative potencies of these agents on the various insulin responsive processes were markedly different. Thus, although these agents have much in common with insulin, the differences in relative potencies suggest that at least some of the insulin-like properties of these compounds may not be exerted through the same mechanisms as insulin.

12/3,AB/42 (Item 42 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03011010 75138083 PMID: 804602
[Prevention of 3,4-benzpyrene carcinogenesis by naturally occurring and synthetic compounds]
Verhinderung der 3,4-Benzopyren-Kanzerogenese
Kallistratos G
MMW. Munchener medizinische Wochenschrift (GERMANY, WEST) Mar 7 1975, 117 (10) p391-4, ISSN 0341-3098 Journal Code: NMM
Languages: GERMAN
Document type: Journal Article
Record type: Completed
The carcinogenic action of 3,4-benzpyrene (3,4-BP) can be reduced or completely inhibited by the presence of substances which occur in the animal organism and also by compounds prepared synthetically. Experiments in female mice have shown that the addition of some unsaturated aliphatic dicarboxylic and tricarboxylic acids, thiols or biogenic amines to 3,4-benzyprene solutions causes a slowing down of the tumor induction or complete blockade of the tumor development. The same 3,4-BP solutions without the addition of the substances mentioned produced malignant tumors in the mice almost without exception.

12/3,AB/43 (Item 43 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02989159 77110533 PMID: 1087858
Chemically defined media for growing anaerobic bacteria of the genus Veillonella.
Lopes JN; Cruz FS
Antonie van Leeuwenhoek (NETHERLANDS) 1976, 42 (4) p411-20, ISSN 0003-6072 Journal Code: 6JE
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A chemically defined medium for Veillonella parvula and V. alcalescens is described. Some nutritional aspects of the two strains used were examined: the optimum concentration of reducing agents, the requirements for amino acids, diamines, vitamins and other growth factors, and the conditions needed for well balanced nutrition. No specific requirements for single amino acids were observed. A combination of L-cysteine, DL-aspartic acid, L-glutamic acid, L-serine and L-tyrosine, promoted growth. In V. alcalescens, serine could substitute both arginine and tryptophan (or histidine). No growth was obtained with ammonium salts as the sole N source. Decarboxylation of L-ornithine, L-lysine and L-arginine was not demonstrated in the Veillonella parvula strain, which required putrescine or cadaverine for growth. Spermine, spermidine, L-lysine, L-ornithine and L-arginine, could not substitute putrescine in Veillonella parvula. Veillonella alcalescens, which does not require putrescine in the medium, was able to decarboxylate L-ornithine while forming putrescine.

12/3,AB/44 (Item 44 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02717842 79223843 PMID: 37501
Reactions of cysteamine and other amine metabolites with glyoxylate and oxygen catalyzed by mammalian D-amino acid oxidase.
Hamilton GA; Buckthal DJ; Mortensen RM; Zerby KW
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jun 1979, 76 (6) p2625-9, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Pig kidney D-amino acid oxidase [D-amino-acid:oxygen oxidoreductase (deaminating), EC 1.4.3.3] catalyzes a rapid uptake of oxygen when high concentrations (50-100 mM) of glyoxylate and the following amines are present under usual assay conditions (pH 8.3): cysteamine, 2-aminoethanol, putrescine, D,L-1-amino-2-propanol, D,L-2-amino-1-propanol, 3-amino-1-propanol, D,L-octopamine, ethylenediamine, and L-cysteine ethyl ester. Notable physiological amines that do not support a rapid O2 reaction under the above conditions include histamine, serotonin, epinephrine, norepinephrine, spermidine, spermine, and cadaverine. A more detailed kinetic investigation of the reactions involving the first four reactive amines listed above indicated that the cysteamine reaction proceeds at a rapid rate even when cysteamine and glyoxylate are present at less than millimolar concentrations, but greater than millimolar concentrations are needed in the other amine reactions in order to observe a reasonable rate. At low concentrations and pH 7.4, the cysteamine-glyoxylate substrate (presumably thiazolidine-2-carboxylic acid) reacts an order of magnitude faster than any other known D-amino acid oxidase substrate. Considerable circumstantial evidence suggests that the reaction involving cysteamine is occurring physiologically, but the reactions of other amines would be occurring in the cell at a very low rate, if at all. It is proposed that the product of the enzymic reaction may be a metabolic effector that can modify the reactivity of proteins or nucleic acids by covalent attachment.

12/3,AB/45 (Item 45 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02055447 72200988 PMID: 4337940
Potentiation of the bradykinin response by cysteine: mechanism of action.
Potter DE; Walaszek EJ
Archives internationales de pharmacodynamie et de therapie (BELGIUM) Jun 1972, 197 (2) p338-49, ISSN 0003-9780 Journal Code: 7EK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

12/3,AB/46 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13349393 BIOSIS NO.: 200100556542
Spermine inhibits DTT potentiation of responses mediated by cysteine mutant recombinant NMDA receptors.
AUTHOR: Herin G A(a); Sinor J D(a); Aizenman E(a)
AUTHOR ADDRESS: (a)Dept Neurobiology, Univ Pitt Sch Med, Pittsburgh, PA** USA
JOURNAL: Society for Neuroscience Abstracts 27 (2):p1848 2001
MEDIUM: print

CONFERENCE/MEETING: 31st Annual Meeting of the Society for Neuroscience
San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We have investigated the action of spermine at NR1/NR2A NMDA receptors expressed in Chinese hamster ovary cells. These studies were aimed at further characterizing the redox properties of NR2A-containing NMDA receptors. We were interested in determining whether polyamines could modify the actions of the reducing agent dithiothreitol (DTT) at a redox modulatory site present in this receptor. The potentiating effects of 4 mM DTT on NMDA (30-100 uM)-induced currents mediated by NR1a/NR2A receptors were unchanged by the presence of 30 uM spermine. However, spermine blocked the effects of DTT by approximately 75% in the cysteine mutant NR1a(c744a,c798a)/NR2A receptor configuration. The overall effects of DTT on NR1a/NR2A and NR1a(c744a,c798a)/NR2A receptors were very similar, as reported previously (Brimecombe et al., JPET 291:785; 1999). Given the prior evidence that the presence of exon 5 in NR1 can mimic certain actions of spermine (Traynelis et al. Science 268:873; 1995), we hypothesized that the exon 5 containing NR1b(c765a,c819a)/NR2A construct would be relatively insensitive to DTT. Cysteines 765 and 819 in NR1b are analogous to cysteines 744 and 798 in NR1a. However, we observed nearly identical DTT sensitivity in the NR1b(c765a,c819a)/NR2A receptor configuration, when compared to the NR1a mutant. In addition, spermine was still able to significantly inhibit the actions of DTT in the NR1b cysteine double mutant. These results suggest that spermine can inhibit the effects of DTT, but only when the redox modulatory site on NR1 has been abolished. In addition, these effects of spermine are not affected by the presence or absence of exon 5.

2001

12/3,AB/47 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12489088 BIOSIS NO.: 200000242590
Chemical potential of Aphelandra sp. cell cultures.
AUTHOR: Nezbedova Lenka; Hesse Manfred; Dusek Jaroslav; Werner Christa(a)
AUTHOR ADDRESS: (a)Organisch-chemisches Institut der Universitat Zurich, Winterthurerstrasse 190, 8057, Zurich**Switzerland
JOURNAL: Plant Cell Tissue and Organ Culture 58 (2):p133-140 1999
ISSN: 0167-6857
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Six different callus lines and three different suspension culture lines were established from plants of two Aphelandra species (Acanthaceae). All established lines were analyzed for secondary metabolite accumulation. A discrepancy between secondary metabolites accumulated in the plants and in the cell cultures could be observed. All established Aphelandra sp. cell cultures produced verbascoside (acteoside) as the major extractable metabolite. Time course experiments were carried out to investigate the relationship between cell growth and verbascoside production. In the present study it was shown that verbascoside accumulation was growth dependent and positively related to the presence of 2,4-D in the medium. The conditions in which verbascoside represents ca. 18% of cell culture weight have been defined. Free

polyamines were detected in the cell culture lines cultivated in MS liquid medium (cysteine 10 mg l-1, thiamine 1 mg l-1, 2,4-D 1 mg l-1, kinetin 0.2 mg l-1 and sucrose 30 g l-1). Putrescine and spermidine accumulated within 8 days to a maximum of 8.4 mumol g-1 of dry wt and 2.6 mumol g-1 of dry wt respectively and thereafter their concentration decreased rapidly. There was no evidence for the presence of spermine or any other type of free or conjugated polyamines in the tested cell culture lines.

1999

12/3,AB/48 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12401346 BIOSIS NO.: 200000154848
Organic solutes protect drought-tolerant Populus X euramericana against reactive oxygen species.
AUTHOR: Guerrier G(a); Brignolas F(a); Thierry C(a); Courtois M(a); Kahlem G(a)
AUTHOR ADDRESS: (a)Biologie des ligneux UFR-Faculte des Sciences, Universite d'Orleans, EA 1207, 45067, Orleans Cedex**France
JOURNAL: Journal of Plant Physiology. 156 (1):p93-99 Jan., 2000
ISSN: 0176-1617
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The mechanisms by which drought-induced oxidative stress is tolerated in poplar were appreciated by the ability of leaf extracts to scavenge reactive oxygen species (ROS) generated in vitro by a xanthine oxidase-hypoxanthine system. Their effects were detected by the protection towards the denaturation of malate dehydrogenase (MDH) of crude and dialysed extracts of a drought-sensitive (Populus X euramericana, Luisa Avanzo) and a drought-tolerant (P. X euramericana, Dorskamp) poplar exposed to control and osmotic stress (-0.336 MPa). At the beginning of the incubation period in presence of ROS, MDH from crude extract of control Dorskamp was protected against the denaturation; boiled crude extracts of control Dorskamp also protected MDH from the dialysed extract of control Luisa Avanzo. In control Dorskamp, cysteine, proline, polyamines and ascorbate added in vitro were efficient ROS scavengers. Compared with the control condition, the rate of MDH denaturation in presence of ROS decreased in a dialysed extract of stressed Luisa Avanzo but increased in that of stressed Dorskamp. Under stress conditions, proline in vitro enhanced the rate of MDH denaturation by ROS in Luisa Avanzo, but competed as ascorbate with ROS in Dorskamp. In Dorskamp, the 12h-exposure to osmotic stress resulted in a decrease in catalase and glutathione reductase activities, in an enhancement of superoxide dismutase, ascorbate peroxidase and contents of some putative leaf antioxidants (putrescine and glutathione), but did not affect the contents of spermine, spermidine and ascorbate. The consequences of extract/solute effects are discussed for each clone as regards the drought response.

2000

12/3,AB/49 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11597085 BIOSIS NO.: 199800377989

Human resource use and habitat availability for red ruffed lemurs, Varecia variegata ruba, in the Anaovandrano River watershed, Masoala Peninsula.
AUTHOR: Vasey N(a)
AUTHOR ADDRESS: (a)Dep. Anthropol., Washington Univ., St. Louis, MO 63130** USA
JOURNAL: Folia Primatologica 69 (SUPPL. 1):p415-416 April, 1998
CONFERENCE/MEETING: International Conference on Biology and Conservation of Prosimians Chester, England, UK September 13-16, 1995
ISSN: 0015-5713
RECORD TYPE: Citation
LANGUAGE: English
1998

12/3,AB/50 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11404661 BIOSIS NO.: 199800185993
Effect of spermine on the phytochelatin concentration and composition in cadmium-treated roots of Canavalia lineata seedlings.
AUTHOR: Yun Il Seong; Hwang In Doo; Moon Byoung Yong; Kwon Young Myung(a)
AUTHOR ADDRESS: (a)Dep. Biol., Res. Center Cell Differentiation, Seoul Natl. Univ., Seoul 151-742**South Korea
JOURNAL: Journal of Plant Biology 40 (4):p275-278 Dec., 1997
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Effect of spermine on the phytochelatins (PCs) in cadmium-treated roots of Canavalia lineata seedlings was studied. With the treatment of spermine, total nonprotein thiol (SH) contents decreased by 55% in roots of Cd-treated plants. Glutathione (GSH) synthetase activity was inhibited by 36.8% in roots and cysteine synthase was also inhibited by 9.5% while gamma-GluCys synthetase activity was not affected. From the PC-Cd complex analyses by gel column chromatography, it was found that Cd+spermine-treated roots contain an additional PC that has low affinity for Cd, in addition to Cd-induced PC whose SH:Cd ratio is 1:1. Spermine affected the PC concentration and composition in the Cd-treated roots of C. lineata seedlings.

1997

12/3,AB/51 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11246193 BIOSIS NO.: 199800027525
Update and evaluation of the effectiveness of different thiols and micellar media in Roth's fluorimetric method for the determination of primary amino compounds.
AUTHOR: Dai Fang; Prelevic Burkert Vera; Singh Hernandon N; Hinze Willie L (a)
AUTHOR ADDRESS: (a)Dep. Chem., Lab. Analytical Med. Micellar, Wake Forest Univ., P.O. Box 7487, Winston-Salem, NC 2**USA
JOURNAL: Microchemical Journal 57 (2):p166-198 Oct., 1997
ISSN: 0026-265X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The reaction time profiles, stabilities, and relative fluorescence responses of isoindoles formed from reaction of 12 different

primary amino compounds with Roth's reagent, i.e., o-phthalaldehyde (OPA) in conjunction with a thiol such as 2-mercaptoethanol (2-ME), 3-mercaptopropionic acid (3-MPA), N-acetyl-L-cysteine (NAC), and 1-thio-D-glucose (TGTA), were determined and discussed in the context of available literature. The effects of surfactant micelles in the derivatization solution were also ascertained. Results indicate that the substitution of either NAC or 3MPA for 2-ME in the OPA reagent formulation leads to superior performance in terms of the isoindole stability and fluorescence response. The addition of surfactant micelles resulted in much greater stability and enhanced fluorescence response for isoindoles formed from reaction of OPA and 2-ME with such primary amines as methylamine, tyramine, aminomethylphosphonic acid, and gamma-aminobutyric acid as well as diamino analytes such as putrescine, spermine, ornithine, and lysine. With 3-MPA or NAC as the thiol in Roth's reagent, the addition of surfactant micelles improved isoindole stability and fluorescence response only for diamino-containing analytes. It is important to realize that the surfactant purity and final surfactant micelle concentration govern the extent by which any micelle system will enhance the isoindole stability and fluorescence response in Roth's method. For derivatizations conducted with TGTA as the thiol, the addition of micelles is not recommended as the resulting isoindole fluorescence response is diminished. It is thought that the favorable micellar effects upon isoindole stability and fluorescence response arises as a consequence of isoindole binding to the micellar aggregate where the molecule experiences a less polar microenvironment (which leads to enhanced fluorescence) and is compartmentalized and isolated within a micelle such that there is a low probability that the same micelle would contain any excess OPA reagent molecules (which leads to improved stability). A brief degradation study revealed that the presence of Brij-35 micellar media enhanced the stability of the isoindole and diminished the rate of its postulated autoxidation degradation reaction.

1997

12/3,AB/52 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09882589 BIOSIS NO.: 199598337507
Asparagine forms a novel adduct with acetaldehyde.
AUTHOR: Park Sang Chul(a); Han Jeong A; Han Jae Gab; Kang Heun Soo
AUTHOR ADDRESS: (a)Dep. Biochem., The WHO Collaborations Cent. Physical Culture and Aging Res. Health Promotion, Se**South Korea
JOURNAL: Korean Journal of Biochemistry 27 (1):p41-45 1995
ISSN: 0378-8512
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Acetaldehyde can form adducts with a variety of biological compounds. In search of acetaldehyde adduct with amino acids and amine compounds, we have found that asparagine can react with acetaldehyde to form a novel adduct nonenzymatically in a dose dependent manner at high pH. By infrared spectrophotometry, 1H-NMR and 13C-NMR spectrometry, the structure of the newly discovered adduct of acetaldehyde-asparagine was identified to be hexahydro-6-oxo-pyrimidine 4-carboxylate. Although its biological significance and adduct formation in vivo remain to be proven, it is possible to hypothesize that asparagine is a novel physiological scavenger of acetaldehyde, which may contribute to prevent or treat the ethanol toxicity.

1995

12/3,AB/53 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09549715 BIOSIS NO.: 199598004633
Reduction in omega-3 fatty acids by UV-B irradiation in microalgae.
AUTHOR: Wang Ken S; Chai Tuu-Jyi(a)
AUTHOR ADDRESS: (a)Horn Point Environ. Lab., Cent. Environ. Estuarine Studies, Univ. Md., Cambridge, MD 21613**USA
JOURNAL: Journal of Applied Phycology 6 (4):p415-421 1994
ISSN: 0921-8971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: UV-B irradiation reduced the levels of omega-3 fatty acid eicosapentaenoic acid (EPA, 20:5-omega-3) and docosahexaenoic acid (DHA, 22:6-omega-3), in microalgae; the degree of reduction varied with species. Chaetoceros calcitrans and Skeletonema costatum were high UV-B tolerant species, followed by Phaeodactylum tricornutum, Chroomonas salina, Pavlova lutheri, and Thalassiosira pseudonana. Isochrysis galbana (T.ISO) and Prorocentrum micans were UV-B sensitive. Cells in logarithmic phase were most sensitive to UV-B irradiation. Nitrate-, phosphate-, or sulphate-starved cells were more UV-B sensitive than non-starved cells grown in a complete basal medium. A relatively short exposure to high UV-B was more damaging than a longer exposure to lower irradiance. Visible light intensity levels had a profound impact on the sensitivity of microalgal cultures to UV-B, with high levels decreasing UV-B dependent damage. Addition of polyamines (putrescine, spermidine or spermine) or an amino acid (cysteine) to the culture medium minimized the reduction of omega-3 fatty acid content in microalgae caused by UV-B irradiation.

1994

12/3,AB/54 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08943684 BIOSIS NO.: 199396095185
Preparation of anti-putrescine antibody and quantitation of putrescine.
AUTHOR: Lee Seung Gwan; Cho Young Dong
AUTHOR ADDRESS: Dep. Biochemistry, Coll. Science, Yonsei Univ., Seoul 120-749**North Korea
JOURNAL: Korean Biochemical Journal 26 (3):p291-297 1993
ISSN: 0368-4881
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Korean; Non-English
SUMMARY LANGUAGE: Korean; English

ABSTRACT: An antibody directed toward putrescine has been produced in rabbits by immunization with a putrescine-protein conjugate which was prepared by a procedure of coupling putrescine to mercaptosuccinylated bovine serum albumin using N-(gamma-maleimidobutyryloxy)succinimide as a coupling agent. In the analysis of ouchterloney double immunodiffusion, anti-putrescine serum produced precipitation line with BSA-putrescine, but not with BSA. Anti-putrescine serum showed 5.3% crossreaction with cadaverine, 3.5% with spermine, and 2.3% with spermidine but not crossreactions with 1,3-diaminopropane and lysine. An radioimmunoassay for putrescine has been developed utilizing anti-putrescine serum bound to nitrocellulose and (1,4-14C)putrescine. The lower limit of detection

by this assay was 100 pmol/tube. In the correlation studies of putrescine determined by this methods (RIA, HPLC, TLC method), RIA showed good correlation with other two methods. This RIA method was turned out to be reproducible, specific, accurate, rapid and simple for determination of putrescine without making derivative of putrescine.

1993

12/3,AB/55 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08380453 BIOSIS NO.: 000094110957
TRITIATED ALPHA AMINO-3-HYDROXY-5-METHYLISOXAZOLE-4-PROPIONIC ACID BINDING TO HUMAN CEREBRAL CORTICAL MEMBRANES MINIMAL CHANGES IN POSTMORTEM BRAINS OF CHRONIC SCHIZOPHRENICS
AUTHOR: KURUMAJI A; ISHIMARU M; TORU M
AUTHOR ADDRESS: DEP. NEUROPSYCHIATRY, TOKYO MED. DENTAL UNIV., 5-45 YUSHIMA 1-CHOME, BUNKYO-KU, TOKYO 113, JPN.
JOURNAL: J NEUROCHEM 59 (3). 1992. 829-837. 1992
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The binding of .alpha.-[3H]amino-3-hydroxy-5-methylisoxazole-4-propionic acid ([3H]AMPA), a selective ligand for the ion channel-linked quisqualate receptor, was evaluated in Triton X-100-treated membranes of human cerebral cortex. The presence of chaotropic ions produced divergent effects on specific [3H]AMPA binding: A twofold increase in the binding was observed with thiocyanide at 100 mM, although iodide (100 mM) and perchlorate (100 mM) reduced the binding. Chemical modifications of the sulfhydryl group with p-chloromercuriphenylsulfonic acid (PCMBS) produced threefold increases in specific [3H]-AMPA binding in the absence of KSCN as well as in the presence of KSCN. Treatment with dithiothreitol restored the enhanced specific [3H]AMPA binding by PCMBS to the basal level. Although specific [3H]AMPA binding in the absence of KSCN showed a single site (KD = 220 nM, Bmax = 235 fmol/mg of protein), curvilinear Scatchard plots of specific [3H]AMPA binding in the presence of 100 mM KSCN can be resolved into two binding sites with the following parameter: KD1 = 5.82 nM, Bmax1 = 247 fmol/mg of protein; KD2 = 214 nM. Bmax2 = 424 fmol/mg of protein. Quisqualate and AMPA were the most potent inhibitors of the [3H]AMPA binding in the presence of KSCN. Potent inhibitors of the binding included .beta.-N-oxalylamino-L-alanine (L-BOAA), cysteine -S-sulfate, L-glutamate, 6-cyano-7-nitroquinoxaline-2,3-dione, and 6,7-dinitroquinoxaline-2,3-dione. Kainate, L-homocysteine sulfinic acid, and L-homocysteic acid were active with an IC50 value of a micromolar concentration, whereas micromolar concentration, whereas L-cysteic acid and L-cysteine sulfinic acid were weakly active. N-Methyl-D-aspartate, L-aspartate, N-acetylaspartylglutamate, quinolinate, and 1-naphthylacetyl spermine, an analogue of Joro spider toxin, were inactive at 1 mM. These results suggest that L-glutamate has an important effect on AMPA receptors in the human cerebral cortex and that L-BOAA and cysteine-S-sulfate exhibit their neurotoxicity through AMPA receptors. Specific [3H]AMPA binding, using the ligand at 6 nM, in the presence of 100 mM KSCN exhibited a heterogeneous distribution pattern in the human cerebral cortex: [3H]AMPA binding values were high in the frontal and occipital cortex, whereas they were low in the parietotemporal cortex. However, no statistically significant changes in [3H]AMPA binding were observed in 22 brain areas of the cerebral cortex of chronic schizophrenics, compared with controls, suggesting that AMPA receptors in the cerebral cortex are minimally

involved in an abnormality of excitatory amino acidergic neurons hypothesized in schizophrenic brain.

1992

12/3,AB/56 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08215186 BIOSIS NO.: 000043015034
POTENTIAL FOR DIETARY CYSTEINE TO ALLEVIATE SPERMINE TOXICITY
AUTHOR: SOUSADIAS M G; SMITH T K
AUTHOR ADDRESS: DEP. NUTR. SCI., UNIV. GUELPH, GUELPH, ONTARIO, CANADA N1G 2W1.
JOURNAL: 1992 MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB), PART II, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J 6 (5). 1992. A1851. 1992
CODEN: FAJOE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1992

12/3,AB/57 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07305907 BIOSIS NO.: 000090085796
THE FORMATION OF CYTOCHROME P-450 FROM CYTOCHROME P-420 IS PROMOTED BY SPERMINE
AUTHOR: HOA G H B; DI PRIMO C; GEZE M; DOUZOU P; KORNBLATT J A; SLIGAR S G
AUTHOR ADDRESS: U310, INSERM, SERV. DE BIOSPECTROSCOPY, INST. DE BIOL. PHYSICO-CHIMIQUE, 13 RU PIERRE ET MARIA CURIE, 75005 PARIS, FRANCE.
JOURNAL: BIOCHEMISTRY 29 (29). 1990. 6810-6815. 1990
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This paper is concerned with camphor-bound bacterial cytochrome P-450 and processes that alter its spin-state equilibrium and influence its transition to the nonactive form, cytochrome P-420, as well as its renaturation to the native camphor-bound cytochrome P-450. Spermine , a polycation carrying a charge of 4+, and potassium, a monovalent cation, were shown to differently cause an increase of high-spin content of camphor-bound cytochrome P-450. The spermine-induced spin transition saturates around 75% of the high spin; a further addition of KCl to the spermine-containing sample shifted the spin state to 95% of the high spin. The volume change of these spin transitions as measured by the use of high pressure indicated an excess of -40 mL/mol for the sample containing potassium as compared to that containing spermine . These results suggest that the proposed privileged site for potassium has not been occupied by spermine and that pressure forces both the camphor and the potassium ion from its sites allowing solvent movement into the protein as well as ordering of solvent by the excluded camphor and potassium. Cytochrome P-420 was produced from cytochrome P-450 by hydrostatic pressure in the presence of potassium, spermine, and cysteine. Potassium cation shows a bigger effect on the stability of cytochrome P-450 than spermine or cysteine, as revealed by a higher value of the pressure of half-inactivation, P1/2, and a bigger inactivation volume change. However, potassium cation did not promote renaturation of cytochrome P-420 to cytochrome P-450 while the presence

of spermine did. The rate of renaturation to cytochrome P-450 was compared with that induced by cysteine, the only previously known effector of P-420 to P-450 interconversion. A probable electrostatic binding site for spermine is suggested and discussed.

1990

12/3,AB/58 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04644554 BIOSIS NO.: 000079057591
CHARACTERIZATION OF D-MYO INOSITOL 1 4 5-TRISPHOSPHATE PHOSPHATASE IN RAT LIVER PLASMA MEMBRANES
AUTHOR: SEYFRED M A; FARRELL L E; WELLS W W
AUTHOR ADDRESS: DEPARTMENT BIOCHEMISTRY, MICHIGAN STATE UNIVERSITY, EAST LANSING, MICH. 48824-1319.
JOURNAL: J BIOL CHEM 259 (21). 1984. 13204-13208. 1984
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: D-myo-Inositol 1,4,5-trisphosphate was previously demonstrated to act as a 2nd messenger for the hormonal mobilization of intracellular Ca in rat liver. The breakdown of D-myo-inositol 1,4,5-trisphosphate by a phosphate activity was characterized. Using partially purified subcellular fractions, D-myo-inositol 1,4,5-trisphosphate phosphatase (I-P3ase) specific activity was highest in the plasma membrane fraction, while D-myo-inositol 1,4-bisphosphate phosphatase specific activity was highest in the cytosolic and microsomal fractions. The plasma membrane I-P3ase was Mg2+-dependent with optimal activity observed at 0.5-1.5 mM free Mg2+. The enzyme had a neutral pH optimum, suggesting that it was neither an acid nor alkaline phosphatase. Neither LiCl nor NaF inhibited the I-P3ase activity. Both L-cysteine and dithiothreitol stimulated the activity 2-fold. Spermine (2.0 mM) inhibited the I-P3ase activity by 50%, while putrescine and spermidine had little or not effect.

1984

12/3,AB/59 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04253855 BIOSIS NO.: 000077079900
EFFECT OF POLY AMINES ON ACIDIFIED ETHANOL INDUCED GASTRIC LESIONS IN RATS
AUTHOR: MIZUI T; DOTEUCHI M
AUTHOR ADDRESS: SHIONOGI RES. LAB., SHIONOGI AND CO., LTD., FUKUSHIMA-KU, OSAKA 553, JPN.
JOURNAL: JPN J PHARMACOL 33 (5). 1983. 939-946. 1983
FULL JOURNAL NAME: Japanese Journal of Pharmacology
CODEN: JJPAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The participation of polyamines and nonprotein sulfhydryls in the gastric cytoprotective mechanisms was studied using gastric mucosal lesions produced by acidified ethanol in rats as an experimental model. Treatment with prostaglandin E2 (PGE2), but not cimetidine, prevented the formation of gastric mucosal lesions. Oral administration of cadaverine, spermidine and spermine prevented the lesion formation by acidified

ethanol in a dose-dependent manner. Indomethacin or acetazolamide had no influence on the cytoprotective effect of spermine, whereas sulfhydryl blockers such as iodoacetamide and N-ethylmaleimide partially blocked it. Sulfhydryl compounds such as cysteine, reduced glutathione (GSH), and cysteamine prevented the lesion formation induced by acidified ethanol. The concentration of nonprotein sulfhydryls in the gastric mucosa was significantly decreased at 1 h after administration of acidified ethanol, and this decrease was partially prevented by spermine or PGE2. The cytoprotective effect of spermine may not be mediated by endogenous PG or alkaline secretion in the gastric mucosa, but may be partially related to endogenous sulfhydryl compounds.

1983

12/3,AB/60 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04235361 BIOSIS NO.: 000077061406
INFLUENCE OF CYSTEINE AND METHIONINE SUPPLEMENTS ON POLY AMINE BIOSYNTHESIS IN THE RAT
AUTHOR: ACUFF R V; SMITH J T
AUTHOR ADDRESS: DEP. SURGERY, EAST TENNESSEE STATE UNIV., JOHNSON CITY, TENN. 37614-0002.
JOURNAL: J NUTR 113 (11). 1983. 2295-2299. 1983
FULL JOURNAL NAME: Journal of Nutrition
CODEN: JONUA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Supplementation of diets containing the optimal level (0.02%) of dietary inorganic sulfate (SO42-) with cysteine instead of methionine can affect several metabolic pathways. It is possible that these results reflect alterations in the biosynthesis of potent physiological compounds, the polyamines. Adult male albino rats were fed diets containing 15% casein and a constant level of inorganic sulfate (0.02%) supplemented with cysteine (0.505% or methionine (0.62%). The polyamines (putrescine, spermidine and spermine) and the controlling enzymes for their biosynthesis ornithine decarboxylase (ODC) and S-adenosylmethionine decarboxylase (SAMD) were evaluated in liver, kidney and brain tissue homogenates following a 17-day dietary period. Rats fed the diet supplemented with cysteine had increased ODC activity and decreased SAMD activity when compared to rats fed diets supplemented with methionine. Polyamine concentrations varied in tissues with a trend toward increasing amounts in animals fed the cysteine -supplemented diet. Dietary cysteine stimulates the biosynthesis and increased tissue concentration of polyamines.

1983

12/3,AB/61 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04141250 BIOSIS NO.: 000027050802
INHIBITION OF AMINO PROPYL TRANSFERASES
AUTHOR: PEGG A E
AUTHOR ADDRESS: DEP. PHYSIOL., MILTON S. HERSHEY MED. CENT., COLL. MED., PENNA. STATE UNIV., HERSHEY, PA 17033.
JOURNAL: TABOR, H. AND C. W. TABOR. METHODS IN ENZYMOLOGY, VOL. 94. POLYAMINES. XXX+497P. ACADEMIC PRESS, INC.: NEW YORK, N.Y., USA. ILLUS. ISBN 3-12-181994-9. 0 (0). 1983. P294-298. 1983

CODEN: MENZA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1983

12/3,AB/62 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03997172 BIOSIS NO.: 000076082738
EFFECT OF ANALOGS OF 5' METHYL THIO ADENOSINE ON CELLULAR METABOLISM INACTIVATION OF S ADENOSYL HOMO CYSTEINE HYDROLASE EC-3.3.1.1 BY 5' ISO BUTYL THIO ADENOSINE
AUTHOR: DELLA RAGIONE F; PEGG A E
AUTHOR ADDRESS: DEP. OF PHYSIOL., MILTON S. HERSHEY MED. CENT., PENNSYLVANIA STATE UNIV. COLL. OF MED., HERSHEY, PA 17033, U.S.A.
JOURNAL: BIOCHEM J 210 (2). 1983. 429-436. 1983
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effects of a number of nucleosides related to 5'-methylthioadenosine on the activities of [rat liver] S-adenosylhomocysteine hydrolase [EC 3.3.1.1], 5'-methylthioadenosine phosphorylase, spermidine synthase and spermine synthase were investigated. Both 5'-methylthioadenosine and 5'-isobutylthioadenosine gave rise to an enzyme-activated irreversible inhibition of S-adenosylhomocysteine hydrolase, but 5'-methylthiotubercidin (5'-methylthio-7-deaza-adenosine), 5'-deoxy-5'-chloroformycin, 5'-ethylthio-2-fluoroadenosine and 1,N6-etheno-5'-methylthioadenosine were totally ineffective in producing this inactivation. Of the nucleosides tested, only 5'-methylthioadenosine, 5'-methylthiotubercidin and 5'-isobutylthioadenosine were inhibitory towards the aminopropyltransferases responsible for the synthesis of spermine and spermidine. 5'-Methylthiotubercidin, 5'-deoxy-5'-chloroformycin and 5'-isobutylthioadenosine were inhibitors of the degradation of 5'-methylthioadenosine by 5'-methylthioadenosine phosphorylase, but only 5'-isobutylthioadenosine was also a substrate for this enzyme. The effects of 5'-isobutylthioadenosine of the cell may result from the combination of inhibitory actions on polyamine synthesis, 5'-methylthioadenosine degradation and S-adenosylhomocysteine degradation. The resulting increased concentrations of S-adenosylhomocysteine could bring about inhibition of methyltransferase reactions. A new convenient method for the assay of S-adenosylhomocysteine hydrolase in the direction of synthesis is described.

1983

12/3,AB/63 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03957663 BIOSIS NO.: 000076043229
BIOSYNTHESIS OF POLY AMINES IN MOUSE BRAIN EFFECTS OF METHIONINE SULFOXIMINE AND ADENOSYL HOMO CYSTEINE
AUTHOR: PROTA R; SCHATZ R A; TATTER S B; SELLINGER O Z
AUTHOR ADDRESS: LAB. NEUROCHEM., MENTAL HEALTH RES. INST., UNIV. MICH. MED. CENT., ANN ARBOR, MICH. 48109, USA.
JOURNAL: J NEUROCHEM 40 (3). 1983. 836-841. 1983
FULL JOURNAL NAME: Journal of Neurochemistry

CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This study examines the consequences on cerebral polyamine biosynthesis of increases and decreases in cerebral methylation. Increases were elicited by administering the convulsant agent methionine sulfoximine (MSO) and decreases by elevating in vivo the cerebral levels of the methylation inhibitor S-adenosyl-homocysteine. Following the intraventricular (i.vt.) administration of one of the two possible polyamine precursors, [1,4-14C]putrescine, the specific radioactivity (SRA) of the newly formed [14C]spermidine remained unchanged. Conversely, after i.vt. L-[3,4-14C]methionine, the other polyamine precursor, significantly higher SRA values for [14C]spermidine and [14C] spermine were recorded in the brains of the MSO-treated animals. [14C]S-adenosylmethionine in the brain of the MSO-treated animals was also more highly labeled following [1-14C]-methionine, indicating its accelerated formation relative to controls. The effect of the administration of adenosine + homocysteine, a treatment that results in elevated brain adenosylhomocysteine levels, on polyamine biosynthesis from [3,4-14C]-methionine was investigated. The results of thse experiments show both significantly lower SRA values for [14C]spermidine and [14C]spermine and sigificantly higher than control endogenous methionine levels, a clear sign of the existence of a retardation in the conversion of methionine to polyamines under these conditions. While interference with cerebral methylation results in significant alterations of the rate of formation of the methionine moiety of spermidine and spermine, it has no effect on the entry of the putrescine moiety into the 2 polyamine molecules.

1983

12/3,AB/64 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03851134 BIOSIS NO.: 000075029207
EFFECT OF SOME OLIGO AMINES AND OLIGO GUANIDINES ON MEMBRANE PERMEABILITY IN HIGHER PLANTS
AUTHOR: SRIVASTAVA S K; SMITH T A
AUTHOR ADDRESS: LONG ASHTON RES. STN., LONG ASHTON, BRISTOL, BS18 9AF, UK.
JOURNAL: PHYTOCHEMISTRY (OXF) 21 (5). 1982. 997-1008. 1982
FULL JOURNAL NAME: PHYTOCHEMISTRY (Oxford)
CODEN: PYTCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of a series of oligo-amines and -guanidines on the membranes of higher plants [Beta vulgaris, Spinacia oleracea, Brassica napobrassica and Malus sylvestris] was tested by measuring the efflux of betacyanin from beet root discs and the loss of total ions from beet root and swede discs, beet and spinach leaf discs and apple cells in suspension culture. All of the naturally occurring di- and polyamines tested showed relatively little toxicity. Betacyanin efflux from beet root discs was reduced by diamines [NH2(CH2)xNH2] up to x = 10 or less. Ion efflux was minimal at x = 7. Within the triamine series [NH2(CH2)xNH(CH2)3NH2] for x = 8 or less, betacyanin efflux was reduced or unaffected, although total ion loss was increased by the triamines when x = 4 or more and especially by the longer chain amines (to x = 10). Similar behavior occurred in the tetra-amine series [NH2(CH2)3NH(CH2)xNH(CH2)3NH2] with betacyanin efflux reduced for x = 2-4 (spermine). Although spermine potentiated the toxicity effects of Guazatine {[NH2C(=NH)NH(CH2)8]2NH} and Dodine

[NH2C(=NH)NH(CH2)11Me] in beet root discs, spermine and Ca2+ reduced the ion efflux caused by these toxic guanidines and also by Synthalin B [NH2C(=NH)NH(CH2)12NHC(=NH)NH2] in swede discs, spinach leaves and apple cells. No significant reversal of ion loss was detected with putrescine, cadaverine or spermidine in swede discs. In the homologous series of monoguanidines [NH2C(=NH)NH(CH2)x-1Me] for x up to 18, greatest toxicity occurred for x = 10 and 11 in both betacyanin loss and total ion efflux in beet root discs. Greatest ion efflux from the apple cell suspension occurred with x = 11 and 12. In the homologus series of diguanidines [NH2C(=NH)NH(CH2)xNHC(=NH)NH2] for x = 2-12 greatest toxicity occurred for x = 12 (the longest chain tested) in beet root and in the efflux of ions from apple cell suspension. Technical Guazatine was considerably more phytotoxic than pure Guazatine in all systems tested. p-Chloromercuribenzoate (p-CMB) potentiates the loss of beta-cyanin and total ions caused by Guazatine, Synthalin B and Dodine in beet root discs. This effect of p-CMB is reversed by subsequent incubation in cysteine or mercaptoethanol, prior to treatment with the guanidines.

1982

12/3,AB/65 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03837955 BIOSIS NO.: 000075016028
CONVERSION OF TYPE II PRO COLLAGEN TO COLLAGEN IN-VITRO REMOVAL OF THE CARBOXY TERMINAL EXTENSION IS INHIBITED BY SEVERAL NATURALLY OCCURRING AMINO-ACIDS POLY AMINES AND STRUCTURALLY RELATED COMPOUNDS
AUTHOR: RYHANEN L; TAN E M L; RANTALA-RYHANEN S; UITTO J
AUTHOR ADDRESS: DIV. DERMATOL., DEP. MED., UCLA SCH. MED., HARBOR UCLA MED. CENT., TORRANCE, CA 90509.
JOURNAL: ARCH BIOCHEM BIOPHYS 215 (1). 1982. 230-236. 1982
FULL JOURNAL NAME: Archives of Biochemistry and Biophysics
CODEN: ABBIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Chick embryo sterna, which actively synthesize type II procollagen, were pulse-labeled with radioactive proline; protein synthesis was then inhibited by unlabeled proline and cycloheximide. After the inhibition of protein synthesis, several amino acids, polyamines, or structurally related compounds were added to the incubation medium. The conversion of procollagen, first to 2 intermediates, pC-collagen and pN-collagen, and then to collagen, was monitored by sodium dodecyl sulfate-polyacrylamide slab gel electrophoresis. The addition of 50 mM .beta.-Ala, Arg, Asn, Gln, hydroxylysine, Lys, or ornithine, as well as agmatine, .epsilon.-aminocaproic acid, S-2-aminoethylcysteine, cadaverine, canavanine, putrescine, or spermine clearly inhibited the removal of the carboxy-terminal extension and pC-collagen accumulated; the removal of the amino-terminal extension was not affected. The inhibition of the conversion was reversible and unaffected by fetal calf serum. The conversion of type II procollagen to collagen may require at least 2 separate proteinases for the removal of amino-terminal and carboxy-terminal extensions. Naturally occurring molecules may be used to modulate the rate of conversion of procollagen to collagen, and development of analogs of these compounds may provide the means to interfere with excessive deposition of collagen in diseases with tissue fibrosis.

1982

12/3,AB/66 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03756691 BIOSIS NO.: 000025009764
THE INFLUENCE OF CYSTEINE AND METHIONINE SUPPLEMENTS UPON POLY AMINE BIOSYNTHESIS IN THE RAT
AUTHOR: ACUFF R V; SMITH J T
AUTHOR ADDRESS: DEP. NUTRITION FOOD SCI., COLL. HOME ECONOMICS AGRIC. EXP. STN., UNIV. TENN., KNOXVILLE, TN 37996-1900.
JOURNAL: 67TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, CHICAGO, ILL., USA, APRIL 10-15, 1983. FED PROC 42 (3). 1983. ABSTRACT 472. 1983
CODEN: FEPRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1983

12/3,AB/67 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03315772 BIOSIS NO.: 000072043876
ROLE OF SULFHYDRYL GROUPS AND POLY AMINES IN CONTROLLING TISSUE PERMEABILITY
AUTHOR: NAIK B I; SRIVASTAVA S K
AUTHOR ADDRESS: BIOCHEM. DEP., M.S. UNIV., BARODA.
JOURNAL: INDIAN J EXP BIOL 19 (5). 1981. 479-480. 1981
FULL JOURNAL NAME: Indian Journal of Experimental Biology
CODEN: IJEBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: SH group binding reagents, iodoacetate and PCMB (p-chloromercuribenzoate) cause a destabilization of membranes in beet root discs resulting in increased betacyanin efflux; spermine causes stabilization. The effects of spermine and PCMB are reversed by cysteine and mercaptoethanol.

1981

12/3,AB/68 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03225221 BIOSIS NO.: 000071038332
VALYL TRANSFER RNA SYNTHETASE FROM YELLOW LUPINE SEEDS HYDROLYSIS OF THE ENZYME BOUND NONCOGNATE AMINOACYL ADENYLATE AS A POSSIBLE MECHANISM OF INCREASING SPECIFICITY OF THE AMINOACYL TRANSFER RNA SYNTHETASE
AUTHOR: JAKUBOWSKI H
AUTHOR ADDRESS: INST. BIOCHEM., AGRIC. UNIV., WOLYNSKA 35, 60-637 POZNAN, POL.
JOURNAL: BIOCHEMISTRY 19 (22). 1980. 5071-5078. 1980
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Lupin valyl-tRNA synthetase catalyzes the hydrolysis of ATP to AMP and pyrophosphate in the absence of tRNA and in the presence of the

following amino acids: cysteine (KM = 22.5 mM; Vrel = 1), threonine (KM = 16 mM; Vrel = 0.2), alanine (KM = 27 mM; Vrel = 0.3), serine (KM = 14 mM; Vrel = 0.12) and .alpha.-aminobutyrate (KM = 1.5 mM; Vrel = 0.1). This activity is due to hydrolysis of the enzyme-bound noncognate aminoacyl adenylates. The enzyme-bound valyl adenylate is apparently protected by the enzyme and slowly decomposes with a rate constant of 0.018 min-1, which is 720 times slower than the rate constant of hydrolysis of valyl-tRNA synthetase-bound cysteinyl adenylate (k = 13 min-1). The KM value for ATP in the ATP pyrophosphohydrolase reaction is 9 .mu.M and does not depend on the nature of the amino acid. This value is one order of magnitude lower than the KM value for ATP in the reaction of tRNA aminoacylation with valine (KM = 100 .mu.M). The cysteine-dependent ATP pyrophosphohydrolase activity of valyl-tRNA synthetase in the absence of tRNA exhibits pH optimum between 9.5 and 10.5 in glycine-NaOH buffer, is moderately sensitive to KCl (50% and 60% inhibition at 150 and 300 mM KCl, respectively), is not affected by 0.1-2 mM spermine, and exhibits a temperature dependence with an Arrhenius energy of activation, Ea = 64.5 kJ, which is the same as that for tRNA aminoacylation with valine. tRNA stimulates the reaction to a degree depending on the nature of amino acid, ATP concentration, pH and kind of buffer used, and KCl and spermine concentrations. Changes of magnesium ion concentration in the range 0.25-10 mM do not affect the stimulation. The degree of stimulation by tRNA of the ATP pyrophosphohydrolase activity also does not depend on temperature. The tRNA apparently acts as an allosteric activator, which binds to the enzyme with Kdiss = 20 nM and increases KM for ATP from 9-100 .mu.M. The KM for amino acids is either not affected (KM = 28 mM for alanine and 14 mM for serine) or slightly affected (KM = 9.6 mM for cysteine and 8.6 mM for threonine) by the presence of tRNA. Transfer RNA devoid of amino acid acceptance by periodate oxidation, albeit able to bind to the enzyme as well as intact tRNA, cannot produce these effects and does not inhibit the ATP pyrophosphohydrolase activity of valyl-tRNA synthetase. Lupin valyl-tRNA synthetase apparently rejects noncognate amino acids at the level of aminoacyl adenylate. The contribution of this pathway of rejection to the overall rejection of noncognate amino acids in the presence of tRNA is calculated to be 25, 19, 12, 2.5 and 2% for cysteine, alanine, serine, threonine and .alpha.-aminobutyrate, respectively.

1980

12/3,AB/69 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03017792 BIOSIS NO.: 000070043410
INHIBITION OF RAT SPERMIDINE SYNTHASE AND SPERMINE SYNTHASE
AUTHOR: HIBASAMI H; BORCHARDT R T; CHEN S Y; COWARD J K; PEGG A E
AUTHOR ADDRESS: DEP. PHYSIOL., SPEC. CANCER RES. CENT., MILTON S. HERSHEY MED. CENT., HERSHEY, PA. 17033, USA.
JOURNAL: BIOCHEM J 187 (2). 1980. 419-428. 1980
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: S-Adenosyl-L-methionine, S-adenosyl-L-homocysteine, 5'-methylthioadenosine and a number of analogs having changes in the base, sugar or amino acid portions of the molecule were tested as potential inhibitors of spermidine synthase and spermine synthase from rat ventral prostate. S-Adenosyl-L-methionine was inhibitory to these reactions, as were other nucleosides containing a sulfonium center. The most active of these were S-adenosyl-L-ethionine,

S-adenosyl-4-methylthiobutyric acid, S-adenosyl-D-methionine and S-tubercidinylmethionine, which were all comparable in activity with S-adenosylmethionine itself, producing 70-98% inhibition at 1 mM concentrations. Spermine synthase was somewhat more sensitive than spermidine synthase. 5'-Methylthioadenosine, 5'-ethylthioadenosine and 5'-methylthiotubercidin were all powerful inhibitors of both enzymes, giving 50% inhibition of spermine synthase at 10-15 .mu.M and 50% inhibition of spermidine synthase at 30-45 .mu.M. S-Adenosyl-L-homocysteine was a weak inhibitor of spermine synthase and practically inactive against spermidine synthase. Analogs of S-adenosylhomocysteine lacking either the carboxy or the amino group acid portion were somewhat more active, as were derivatives in which the ribose ring had been opened by oxidation. The sulfoxide and sulfone derivatives of decarboxylated S-adenosyl-L-homocysteine and the sulfone of S-adenosyl-L-homocysteine were potent inhibitors and were particularly active against spermidine synthase (giving 50% inhibition at 380, 50 and 20 .mu.M, respectively). These results are discussed in terms of the possible regulation of polyamine synthesis by endogenous nucleosides and the possible value of some of the inhibitory substances in experimental manipulations of polyamine concentrations. 5'-Methylthiotubercidin and the sulfone of S-adenosylhomocysteine or of S-adenosyl-3-thiopropylamine may be particularly valuable in this respect.

1980

12/3,AB/70 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03012438 BIOSIS NO.: 000070038056
METHIONINE METABOLISM IN WALKER CARCINO SARCOMA IN-VITRO
AUTHOR: TISDALE M J
AUTHOR ADDRESS: DEP. BIOCHEM., ST. THOMAS HOSP. MED. SCH., LONDON SE1 7EH, ENGL., UK.
JOURNAL: EUR J CANCER 16 (3). 1980. 407-414. 1980
FULL JOURNAL NAME: European Journal of Cancer
CODEN: EJCAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: When homocysteine (0.1-0.3 mM) replaced methionine in media supplemented with folic acid (0.01-0.1 mM) and hydroxocobalamin (0.1-7.5 .mu.M) there was no growth of [rat] Walker carcinoma in tissue culture. These cells were also unable to grow when supplemented with 5-methyl (10-50 .mu.M) or 5-formyltetrahydrofolic acid (10-40 .mu.g/ml), S-adenosyl-L-methionine (200 .mu.M), S-methylcysteine (0.05-0.5 mM), 5-deoxy-5'-methylthioadenosine (0.05-0.5 mM), S-(methanethiol)-L-cysteine (0.1-1.0 mM), L-cystine (0.1-1.0 mM) or with added spermine (0.2-1.0 .mu.g/ml) plus spermidine (0.15-0.75 .mu.g/ml). The inability of Walker carcinoma to grow in methionine-deficient media was not due to a loss of 5-methyltetrahydrofolate or L-homocysteine S-methyl transferase since not only was the activity of this enzyme comparable with that found in [mouse] TLX5 lymphoma, which proliferated in methionine-deficient media supplemented with homocysteine, but there was also a 6-fold induction of enzyme activity during 48 h incubation in such deficient media. The activity of the methyltransferase was proportional to the methionine concentration in the medium. There was no appreciable alteration in the number of surface sulfhydryl groups in homocysteine-supplemented media. The inability of Walker carcinoma to proliferate in methionine-depleted, homocysteine-supplemented media apparently is not due to any innate biochemical defect and may be due to a higher methionine requirement of this cell line.

1980

12/3,AB/71 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02756299 BIOSIS NO.: 000068066906
REACTIONS OF CYSTEAMINE AND OTHER AMINE METABOLITES WITH GLYOXYLATE AND OXYGEN CATALYZED BY MAMMALIAN D AMINO-ACID OXIDASE EC-1.4.3.3
AUTHOR: HAMILTON G A; BUCKTHAL D J; MORTENSEN R M; ZERBY K W
AUTHOR ADDRESS: DEP. CHEM., PA. STATE UNIV., UNIVERSITY PARK, PA. 16802, USA.
JOURNAL: PROC NATL ACAD SCI U S A 76 (6). 1979. 2625-2629. 1979
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Pig kidney D-amino acid oxidase [D-amino-acid:oxygen oxido reductase (deaminating), EC 1.4.3.3] catalyzes a rapid uptake of O2 when high concentrations (50-100 mM) of glyoxylate and the following amines are present under usual assay conditions (pH 8.3): cysteamine, 2-aminoethanol, putrescine, D,L-1-amino-2-propanol, D,L-2-amino-1-propanol, 3-amino-1-propanol, D,L-octopamine, ethylenediamine and L-cysteine ethyl ester. Notable physiological amines that do not support a rapid O2 reaction under the above conditions include histamine, serotonin, epinephrine, norepinephrine, spermidine, spermine and cadaverine. A more detailed kinetic investigation of the reactions involving the first 4 reactive amines listed above indicated that the cysteamine reaction proceeds at a rapid rate even when cysteamine and glyoxylate are present at less than mM concentrations, but greater than mM concentrations are needed in the other amine reactions in order to observe a reasonable rate. At low concentrations and pH 7.4, the cysteamine-glyoxylate substrate (presumably thiazolidine-2-carboxylic acid) reacts an order of magnitude faster than any other known D-amino acid oxidase substrate. Considerable circumstantial evidence suggests that the reaction involving cysteamine is occurring physiologically, but the reactions of other amines should be occurring in the cell at a very low rate, if at all. The product of the enzymic reaction may be a metabolic effector that can modify the reactivity of proteins or nucleic acids by covalent attachment.

1979

12/3,AB/72 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02652877 BIOSIS NO.: 000067040942
METHYLATION OF ESCHERICHIA-COLI TRANSFER RNA BY A TRANSFER RNA ADENINE 1 METHYL TRANSFERASE EC-2.1.1.36 FROM RAT BRAIN CORTEX AND BULK ISOLATED NEURONS
AUTHOR: SALAS C E; SELLINGER O Z
AUTHOR ADDRESS: LAB. NEUROCHEM., MENT. HEALTH RES. INST., UNIV. MICH. MED. CENT., 205 WASHTENAW PL., ANN ARBOR, MICH. 48109, USA.
JOURNAL: J NEUROCHEM 31 (1). 1978. 85-92. 1978
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Brain cortices or bulk-isolated neuronal cell bodies prepared from cortices of 8 day old male rats were used as the source of a 1-methyl adenine-specific tRNA methyltransferase [EC 2.1.1.36] (tRNA-AMT). Ammonium sulfate fractionation and chromatography on spheroidal hydroxylapatite and Sephadex G-200 yielded an 80-fold purified enzyme, as determined by using E. coli bulk tRNA as substrate. The kinetic parameters of tRNA-AMT for the substrate S-adenosyl-L-methionine (Km = 6 .mu.M) and the inhibitor, S-adenosyl-L-homocysteine (SAH) (Ki = 3.4 .mu.M) were determined and several SAH analogs tested as inhibitors. S-Adenosyl-L-cysteine (10-4M) and S-adenosyl-D-homocysteine (10-4M) produced a 35 and a 21% reduction in enzyme activity, respectively. The effects of Mg2+, .**GRAPHIC**. acetate and of the polyamines spermine, putrescine and spermidine on the brain tRNA-AMT mimicked the effects of these agents on hepatic tRNA-AMT. Comparing the ability of cerebral tRNA-AMT to methylate E. coli tRNAglu2, tRNAval, tRNAphe and bulk tRNA revealed tRNAglu2, as the best and tRNAphe as the least effective substrate. tRNA-AMT prepared from neuronal cell bodies showed closely similar characteristics to the cortical enzyme. A comparison of the activities of tRNA-AMT in neurons and glial cells revealed higher values in the former.

1978

12/3,AB/73 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02514313 BIOSIS NO.: 000016022369
METHIONINE AND POLY AMINE METABOLISM IN THE BRAIN AND LIVER OF THE DEVELOPING HUMAN AND RHESUS MONKEY
AUTHOR: STURMAN J A; GAULL G E
JOURNAL: CAMPBELL, ROBERT A. ET AL. (ED.). ADVANCES IN POLY AMINE RESEARCH, VOL. 2. XVII+377P. ILLUS. RAVEN PRESS: NEW YORK, N.Y., USA. ISBN 0-89004-194-6. 1978 213-240 1978
CODEN: 06531
RECORD TYPE: Citation
1978

12/3,AB/74 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02125734 BIOSIS NO.: 000063040730
A NEW METHOD FOR THE ASSAY OF TISSUE S ADENOSYL HOMO CYSTEINE AND S ADENOSYL METHIONINE EFFECT OF PYRIDOXINE DEFICIENCY ON THE METABOLISM OF S ADENOSYL HOMO CYSTEINE S ADENOSYL METHIONINE AND POLY AMINES IN RAT LIVER
AUTHOR: ELORANTA T O; KAJANDER E O; RAINA A M
JOURNAL: BIOCHEM J 160 (2). 1976 287-294. 1976
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract

ABSTRACT: The hepatic synthesis and accumulation of S-adenosylhomocysteine, S-adenosylmethionine and polyamines were studied in normal and vitamin B-6-deficient male albino rats. A method involving a single chromatography on a phosphocellulose column was developed for the determination of S-adenosylhomocysteine and S-adenosylmethionine from tissue samples. Feeding the rat with pyridoxine-deficient diet for 3 or 6 wk resulted in a 4- to 5-fold increase in the concentration of S-adenosylhomocysteine; that of S-adenosylmethionine was only slightly elevated. The concentration of putrescine was decreased to half, that of

spermidine was somewhat decreased and that of spermine remained fairly constant. The activities of L-ornithine decarboxylase, S-adenosyl-L-methionine decarboxylase, L-methionine adenosyltransferase and S-adenosyl-L-homocysteine hydrolase were moderately increased. S-Adenosylmethionine decarboxylase showed no requirement for pyridoxal 5'-phosphate. The major effect of pyridoxine deficiency on S-adenosylmethionine metabolism seems to be a block in the utilization of S-adenosylhomocysteine, resulting in the accumulation of this metabolite to a concentration that may inhibit biological methylation reactions.

1976

12/3,AB/75 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01988867 BIOSIS NO.: 000013008984
CONTROL OF PROTEIN PHOSPHORYLATION BY CYCLIC NUCLEOTIDES
AUTHOR: NISHIZUKA Y
JOURNAL: J BIOCHEM (TOKYO) 79 (4). 1976 42P 1976
FULL JOURNAL NAME: Journal of Biochemistry (Tokyo)
CODEN: JOBIA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
1976

12/3,AB/76 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01297357 BIOSIS NO.: 000010037590
ACROLEIN FORMATION IN AEROBIC INTERACTIONS OF METHIONINE OR SPERMINE WITH RIBOSE AND FROM RELATED COMPOUNDS
AUTHOR: ALARCON R A; MELENDEZ L V
JOURNAL: FED PROC 33 (3 PART 1). 1974 681 1974
FULL JOURNAL NAME: Federation Proceedings
CODEN: FEPRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
1974

12/3,AB/77 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01017921 BIOSIS NO.: 000054068131
POTENTIATION OF THE BRADY KININ RESPONSE BY CYSTEINE MECHANISM OF ACTION
AUTHOR: POTTER D E; WALASZEK E J
JOURNAL: ARCH INT PHARMACODYN THER 197 (2). 1972 338-349. 1972
FULL JOURNAL NAME: Archives Internationales de Pharmacodynamie et de Therapie
CODEN: AIPTA
RECORD TYPE: Citation
1972

12/3,AB/78 (Item 33 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

00714197 BIOSIS NO.: 000052074236
THE EFFECTS OF SPERMINE SPERMIDINE CALCIUM CHLORIDE AND CYSTEINE HYDANTOIN ON THE SHRINKING AND SWELLING OF CELLS OF A STRAIN OF PSEUDOMONAS-AERUGINOSA EXPOSED TO HEAT OR STREPTOMYCIN
AUTHOR: BERNHEIM F
JOURNAL: MICROBIOS 2 (7-8). 1970 261-267. 1970
FULL JOURNAL NAME: Microbios
CODEN: MCBIA
RECORD TYPE: Citation
1970

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       20863023  PY<1998
     S16      658  LIPOSOM? AND REVIEW? AND PY<1998
? s s16 and py>1994

             658  S16
         6936118  PY>1994
     S17      176  S16 AND PY>1994
? rd

...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...completed examining records
     S18      139  RD (unique items)
? s s18 and cystein?

             139  S18
          100322  CYSTEIN?
     S19        0  S18 AND CYSTEIN?
? s s18 and c10

             139  S18
            3201  C10
     S20        0  S18 AND C10
? s c10 and cystein?

            3201  C10
          100322  CYSTEIN?
     S21       53  C10 AND CYSTEIN?
? rd

...examined 50 records  (50)
...completed examining records
     S22       36  RD (unique items)
? t s22/3,ab/all


 22/3,AB/1      (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12925370   21408716   PMID: 11517925
  Evolutionary lines of cysteine peptidases.
  Barrett A J; Rawlings N D
  MRC Molecular Enzymology Laboratory, The Babraham Institute,
Cambridgeshire, UK.
  Biological chemistry (Germany) May 2001, 382 (5) p727-33, ISSN
1431-6730  Journal Code: 9700112
  Languages: ENGLISH
  Document type: Journal Article; Review; Review, Tutorial
  Record type: Completed
  The proteolytic enzymes that depend upon a cysteine residue for
activity have come from at least seven different evolutionary origins, each
of which has produced a group of cysteine peptidases with distinctive
structures and properties. We show here that the characteristic molecular
topologies of the peptidases in each evolutionary line can be seen not only
in their three-dimensional structures, but commonly also in the
two-dimensional structures. Clan CA contains the families of papain (C1),
calpain (C2), streptopain (C10) and the ubiquitin-specific peptidases
(C12, C19), as well as many families of viral cysteine
endopeptidases. Clan CD contains the families of clostripain (C11),
gingipain R (C25), legumain (C13), caspase-1 (C14) and separin (C50). These
enzymes have specificities dominated by the interactions of the S1 subsite.
Clan CE contains the families of adenain (C5) from adenoviruses, the
eukaryotic Ulp1 protease (C48) and the bacterial YopJ proteases (C55). Clan
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CF contains only pyroglutamyl peptidase I (C15). The picornains (C3) in clan PA have probably evolved from serine peptidases, which still form the majority of enzymes in the clan. The cysteine peptidase activities in clans PB and CH are autolytic only. In conclusion, we suggest that although almost all the cysteine peptidases depend for activity on catalytic dyads of cysteine and histidine, it is worth noting some important differences that they have inherited from their distant ancestral peptidases.

22/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11832806 21547368 PMID: 11687939
A moderate amplification of the mecB gene encoding cystathionine-gamma-lyase stimulates cephalosporin biosynthesis in Acremonium chrysogenum.
Kosalkova K; Marcos A T; Martin J F
Area de Microbiologia, Facultad de Ciencias Biologicas y Ambientales, Universidad de Leon, Leon 24071, Spain.
Journal of industrial microbiology & biotechnology (England) Oct 2001, 27 (4) p252-8, ISSN 1367-5435 Journal Code: CTU
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
L-cysteine is a precursor of the penicillin, cephalosporin and cephamycin families of beta-lactam antibiotics. Cystathionine-gamma-lyase (encoded by the mecB gene), an enzyme that splits cystathionine releasing cysteine , is required for high-level cephalosporin production in methionine-supplemented medium. By amplification of the mecB gene in Acremonium chrysogenum C10, several transformants were obtained that produced 10-40% higher levels of cephalosporin. All selected transformants contained at least two or three copies of the mecB gene as shown by Southern hybridization with a probe internal to mecB. Two of these transformants, A. chrysogenum T27 and A. chrysogenum T58, showed 4- to 10-fold higher cystathionine-gamma-lyase activity than the control strain. Northern hybridizations indicated that the levels of the two mecB transcripts of 1.7 and 1.5 kb were greatly increased in transformants T27 and T58. Fermentor studies using controlled conditions confirmed that transformant T27 was a cephalosporin overproducer, reaching titers of nearly 2000 microg/ml of cephalosporin in Shen-defined medium that correlated with two- to fourfold higher cystathionine-gamma-lyase levels than in the control strain. Transformant T58 containing five- to sixfold higher levels of cystathionine-gamma-lyase in fermentor cultures showed a reduced growth rate and a slow cephalosporin accumulation rate. In conclusion, moderately increased levels of cystathionine-gamma-lyase stimulated cephalosporin production but very high levels of this enzyme were deleterious for growth and cephalosporin biosynthesis.

22/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11783864 21540691 PMID: 11683639
Pegylation: a method for assessing topological accessibilities in kv1.3.
Lu J; Deutsch C
Department of Physiology, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6085.
Biochemistry (United States) Nov 6 2001, 40 (44) p13288-301, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
Each subunit of a voltage-gated potassium channel (Kv) contains six

putative transmembrane segments, S1-S6, and a cytosolic N-terminal recognition domain, T1. Although it is well-established that Kv channels are tetrameric structures, the protein-protein, protein-lipid, and protein-aqueous interfaces are not precisely mapped. The topological accessibility of specific amino acids may help to identify these border residues. Toward this end, a variant of the substituted-cysteine -accessibility method that relies on mass-labeling of accessible SH groups with a large SH reagent, methoxy-polyethylene glycol maleimide, and gel shift assay has been used. Pegylation of full-length Kv1.3, as well as Kv1.3 fragments, integrated into microsomal membranes, allows topological characterization of the 12 native cysteines (C1-C12), as well as cysteines engineered into a T1-T1 interface. Cysteines engineered into the T1-T1 interface had lower rates of pegylation than cytosolic-facing cysteines, namely, C5 in the T1 domain and C10 -C12 in the C terminus.

22/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11485591 21225049 PMID: 11325719
Mechanism underlying slow kinetics of the OFF gating current in Shaker potassium channel.
Melishchuk A; Armstrong CM
Department of Physiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104, USA. melischu@mai.med.upenn.edu
Biophysical journal (United States) May 2001, 80 (5) p2167-75, ISSN 0006-3495 Journal Code: A5S
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Based on the structure of the KcsA potassium channel, the Shaker K+ channel is thought to have, near the middle of the membrane, a cavity that can be occupied by a permeant or a blocking cation. We have studied the interaction between cations in the cavity and the activation gate of the channel, using a set of monovalent cations together with Shaker mutants that modify the structure of the cavity. Our results show that reducing the size of the side chain at position 470 makes it possible for the mutant channel, unlike native Shaker, to close with tetraethylammonium (TEA+) or the long-chain TEA-derivative C10 + trapped inside the channel. Neither I470 mutants nor Shaker can close when N-methyl-glucamine (NMG+) is in the channel, even though this ion is smaller than C10 +. Apparently, the carbohydrate side chain of NMG+ prevents gate closing. Gating currents recorded from Shaker and I470C were measured in the presence of different intracellular cations to further analyze the interaction of cations with the gate. Our results suggest that the cavity in Shaker is so small that even permeant cations like Rb+ or Cs+ must leave the cavity before the channel gate can close.

22/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11182140 21148767 PMID: 11254121
Characterization of the reverse transsulfuration gene mecB of Acremonium chrysogenum, which encodes a functional cystathionine-gamma-lyase.
Marcos AT; Kosalkova K; Cardoza RE; Fierro F; Gutierrez S; Martin JF
Instituto de Biotecnologia INBIOTEC, Parque Cientifico de Leon, Spain. degjmm@unileon.es
Molecular & general genetics (Germany) Feb 2001, 264 (6) p746-54, ISSN 0026-8925 Journal Code: NGP
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

In Acremonium chrysogenum, biosynthesis of cysteine for the formation of cephalosporin has been proposed to occur through the reverse transsulfuration pathway. A gene, named mecB, has been cloned from an A. chrysogenum C10 genomic library in lambdaEMBL3-ble. The cloned DNA fragment encodes a protein of 423 amino acids with a deduced molecular mass of 45 kDa that shows great similarity to cystathionine-gamma-lyases from Saccharomyces cerevisiae and other eukaryotic organisms. The protein was shown to be functional because it restores growth on methionine to A. nidulans C47 (mecB10), a mutant that is known to be defective in cystathionine-gamma-lyase. The cloned gene did not complement A. nidulans mecA or metG mutants. Enzyme activity assays confirmed that the cloned mecB gene encodes a cystathionine-gamma-lyase activity. The mecB gene is present in a single copy in the wild-type A. chrysogenum (Brotzu's strain) and also in the A. chrysogenum strain C10, a high cephalosporin producer. The gene is localized on chromosome VIII (5.3 Mb), as shown by hybridization to A. chrysogenum chromosomes resolved by pulsed-field gel electrophoresis. Transcription of the mecB gene gives rise to a major transcript of 1.5 kb and a minor one of 1.7 kb. The transcript levels were not significantly affected by addition of DL-methionine to the culture, indicating that expression of this gene is not regulated by methionine. The availability of this gene provides a very useful tool for understanding the proposed role of cystathionine-gamma-lyase in splitting cystathionine to supply cysteine for cephalosporin biosynthesis.

22/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11137956 21101871 PMID: 11160109

Targeted inactivation of the mecB gene, encoding cystathionine-gamma-lyase, shows that the reverse transsulfuration pathway is required for high-level cephalosporin biosynthesis in Acremonium chrysogenum C10 but not for methionine induction of the cephalosporin genes.

Liu G; Casqueiro J; Banuelos O; Cardoza RE; Gutierrez S; Martin JF

Area of Microbiology, Faculty of Biology, University of Leon, 24071 Leon, Spain.

Journal of bacteriology (United States) Mar 2001, 183 (5) p1765-72, ISSN 0021-9193 Journal Code: HH3

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Targeted gene disruption efficiency in Acremonium chrysogenum was increased 10-fold by applying the double-marker enrichment technique to this filamentous fungus. Disruption of the mecB gene by the double-marker technique was achieved in 5% of the transformants screened. Mutants T6 and T24, obtained by gene replacement, showed an inactive mecB gene by Southern blot analysis and no cystathionine-gamma-lyase activity. These mutants exhibited lower cephalosporin production than that of the control strain, A. chrysogenum C10 , in MDFA medium supplemented with methionine. However, there was no difference in cephalosporin production between parental strain A. chrysogenum C10 and the mutants T6 and T24 in Shen's defined fermentation medium (MDFA) without methionine. These results indicate that the supply of cysteine through the transsulfuration pathway is required for high-level cephalosporin biosynthesis but not for low-level production of this antibiotic in methionine-unsupplemented medium. Therefore, cysteine for cephalosporin biosynthesis in A. chrysogenum derives from the autotrophic (SH(2)) and the reverse transsulfuration pathways. Levels of methionine induction of the cephalosporin biosynthesis gene pcbC were identical in the parental strain and the mecB mutants, indicating that the induction effect is not mediated by cystathionine-gamma-lyase.

22/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11085563 21102794 PMID: 11182766
Expression, purification and characterization of the structure and disulfide linkages of insulin-like growth factor binding protein-4.
Chelius D; Baldwin MA; Lu X; Spencer EM
Department of Growth and Development, California Pacific Medical Center Research Institute, San Francisco, California 94114, USA.
Journal of endocrinology (England) Feb 2001, 168 (2) p283-96, ISSN 0022-0795 Journal Code: I1J
Contract/Grant No.: GM 17345, GM, NIGMS; RR 01614, RR, NCRR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Insulin-like growth factor binding protein-4 (IGFBP-4), like the other five IGFBPs, is a critical regulator of the activity of insulin-like growth factor (IGF)-I and IGF-II. However IGFBP-4 seems to be the only IGFBP with no potential to enhance the mitogenic actions of the IGFs. IGFBP-1 to -3 and -5 each contain 18 conserved cysteine residues, IGFBP-6 lacks two of the twelve N-terminal cysteines, while IGFBP-4 has two additional cysteines in the central region. A plasmid was constructed to express rat IGFBP-4 as a thioredoxin fusion protein that included a hexahistidine sequence to permit affinity purification. The fusion protein was expressed in E.coli, purified using nickel-chelate affinity chromatography and cleaved by tobacco etch virus (TEV) protease to produce mature rat IGFBP-4 with an additional glycine residue at the N-terminus. Final purification was achieved by further nickel affinity chromatography and reverse phase HPLC. The isoelectric points of the recombinant IGFBP-4 were the same as those of the non-glycosylated isoforms of IGFBP-4 in rat serum. The binding affinities of the recombinant protein and IGFBP-4 secreted by rat cells to IGF-I were compared using a newly developed binding assay. No significant difference could be detected, consistent with proper folding of the recombinant protein. This indicates that glycosylation of IGFBP-4 does not affect its binding to IGF-I. Using mass spectrometry and tandem mass spectrometry no differences between authentic and recombinant IGFBP-4 could be detected. Eight of the ten disulfide linkages have been determined, including linkages of conserved cysteine residues not previously identified in other IGFBPs. Numbering the cysteine residues sequentially from the N-terminus only the disulfide connectivity of C1, C2, C5 and C6 could not be determined. However, C1 is not linked to C1 and C5 is not linked to C6. The established linkages were C3 to C8, C4 to C7, C9 to C 11, and C10 to C12. The two cysteines in the non-conserved mid-region unique to IGFBP-4 (C13 and C14) are linked together. Linkage of the C-terminal cysteine residues is identical to that of IGFBP-2, -5 and -6 (C15 to C16, C17 to C18 and C19 to C20). The central flexible core of IGFBP-4, containing two additional cysteines may contribute to its unique biological action.

22/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10807753 99367391 PMID: 10436176
The complete primary structure of mouse 20S proteasomes.
Elenich LA; Nandi D; Kent AE; McCluskey TS; Cruz M; Iyer MN; Woodward EC; Conn CW; Ochoa AL; Ginsburg DB; Monaco JJ
Howard Hughes Medical Institute, and Departments of Molecular Genetics and Cell Biology, University of Cincinnati, 231 Bethesda Avenue, Cincinnati, OH 45267-0524, USA.
Immunogenetics (UNITED STATES) Sep 1999, 49 (10) p835-42, ISSN 0093-7711 Journal Code: GI4
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
The proteasome is a large multicatalytic proteinase that plays a role in the generation of peptides for presentation by major histocompatibility complex class I molecules. The 20S proteolytic core of mammalian proteasomes is assembled from a group of 17 protein subunits that generate a distinctive pattern of spots upon two-dimensional gel electrophoresis. The genes for most of these subunits have been cloned from humans and rats. We isolated cDNA clones for the mouse orthologues of ten of the subunits [PSMA1 (C2), PSMA2 (C3), PSMA3 (C8), PSMA4 (C9), PSMA5 (ZETA), PSMA6 (IOTA), PSMA7 (C6-I), PSMB2 (C7-I), PSMB3 (C10-II), and PSMB5 (X)] to complete the cloning of all of the mouse subunits. Using antisera raised against these subunits or their orthologues, we verified the identity of these proteins by two-dimensional NEPHGE-PAGE.

22/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10386571 20042588 PMID: 10572006
Membrane assembly of the 16-kDa proteolipid channel from Nephrops norvegicus studied by relaxation enhancements in spin-label ESR.
Pali T; Finbow ME; Marsh D
Max-Planck-Institut fur biophysikalische Chemie, Abteilung Spektroskopie, Gottingen, Germany.
Biochemistry (UNITED STATES) Oct 26 1999, 38 (43) p14311-9, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The 16-kDa proteolipid from the hepatopancreas of Nephrops norvegicus belongs to the class of channel proteins that includes the proton-translocation subunit of the vacuolar ATPases. The membranous 16-kDa protein from Nephrops was covalently spin-labeled on the unique cysteine Cys54, with a nitroxyl maleimide, or on the functionally essential glutamate Glu140, with a nitroxyl analogue of dicyclohexylcarbodiimide (DCCD). The intensities of the saturation transfer ESR spectra are a sensitive indicator of spin-spin interactions that were used to probe the intramembranous structure and assembly of the spin-labeled 16-kDa protein. Spin-lattice relaxation enhancements by aqueous Ni(2+) ions revealed that the spin label on Glu140 is located deeper within the membrane (around C9-C10 of the lipid chains) than is that on Cys54 (located around C5-C6). In double labeling experiments, alleviation of saturation by spin-spin interactions with spin-labeled lipids indicates that spin labels both on Cys54 and on Glu140 are at least partially exposed to the lipid chains. The decrease in saturation transfer ESR intensity observed with increasing spin-labeling level is evidence of oligomeric assembly of the 16-kDa monomers and is consistent with a protein hexamer. These results determine the locations and orientations of transmembrane segments 2 and 4 of the 16-kDa putative 4-helix bundle and put constraints on molecular models for the hexameric assembly in the membrane. In particular, the crucial DCCD-binding site that is essential for proton translocation appears to contact lipid.

22/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10341239 99376271 PMID: 10449041
The disulfide bond arrangement in the extracellular domain of the activin type II receptor.
Fischer WH; Greenwald J; Park M; Craig AG; Choe S; Vale W
The Clayton Foundation Laboratories for Peptide Biology, The Salk Institute, La Jolla, California 92037, USA. Fischer@salk.edu
Journal of protein chemistry (UNITED STATES) May 1999, 18 (4)

p437-46, ISSN 0277-8033 Journal Code: AEJ
Contract/Grant No.: 1 S10 RR 08425-01, RR, NCRR; 1 S10 RR 11404-01, RR, NCRR; HD13527, HD, NICHD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The initial step in the signaling cascade of the growth factor activin involves its binding to the extracellular domain of the activin type II receptor. This receptor domain contains 10 cysteine residues which are engaged in intramolecular disulfide bonds. To elucidate the structural framework of this domain we have characterized its disulfide-bonding pattern using an extracellular fragment of the receptor which binds activin A with high affinity. By combining proteolysis with mass spectroscopy and chemical sequence analysis, the disulfide connectivity was determined to be as follows: C1-C3, C2-C4, C5-C8, C6-C7, and C9-C10 . A similar disulfide arrangement occurs in a family of snake toxins for which the three-dimensional structure is known.

22/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10302769 98223637 PMID: 9554881
Clarification of the binding mode of teleocidin and benzolactams to the Cys2 domain of protein kinase Cdelta by synthesis of hydrophobically modified, teleocidin-mimicking benzolactams and computational docking simulation.
Endo Y; Takehana S; Ohno M; Driedger PE; Stabel S; Mizutani MY; Tomioka N ; Itai A; Shudo K
Graduate School of Pharmaceutical Sciences, University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113, Japan. yendo@mol.f.u-tokyo.ac.jp
Journal of medicinal chemistry (UNITED STATES) Apr 23 1998, 41 (9) p1476-96, ISSN 0022-2623 Journal Code: J0F
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Phorbol esters (12-O-tetradecanoylphorbol 13-acetate; TPA) and teleocidins are known to be potent tumor promoters and to activate protein kinase C (PKC) by binding competitively to the enzyme. The relationship between the chemical structures and the activities of these compounds has attracted much attention because of the marked structural dissimilarities. The benzolactam 5, with an eight-membered lactam ring and benzene ring instead of the nine-membered lactam ring and indole ring of teleocidins, reproduces the active ring conformation and biological activities of teleocidins. Herein we describe the synthesis of benzolactams with hydrophobic substituents at various positions. Structure-activity data indicate that the existence of a hydrophobic region between C-2 and C-9 and the steric factor at C-8 play critical roles in the appearance of biological activities. We also computationally simulated the docking of teleocidin and the modified benzolactam molecules to the Cys2 domain structure observed in the crystalline complex of PKCdelta with phorbol 13-acetate. Teleocidin and benzolactams fitted well into the same cavity as phorbol 13-acetate. Of the three functional groups hydrogen-bonding to the protein, two hydrogen-bonded with protein atoms in common with phorbol 13-acetate, but the third one hydrogen-bonded with a different protein atom from that in the case of phorbol 13-acetate. The model explains well the remarkable difference in activity between 5 and its analogue having a bulky substituent at C-8.

22/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10302043 98222589 PMID: 9545527

Stringent structural requirements for anti-Ras activity of S-prenyl analogues.

Aharonson Z; Gana-Weisz M; Varsano T; Haklai R; Marciano D; Kloog Y
Department of Neurobiochemistry, George S. Wise Faculty of Life Sciences, Tel-Aviv University, Israel.

Biochimica et biophysica acta (NETHERLANDS) Feb 27 1998, 1406 (1) p40-50, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The carboxy terminal S-farnesylcysteine of Ras oncoproteins is required for their membrane anchorage and transforming activities. We showed previously that S-farnesylthiosalicylic acid (FTS) affects the membrane anchorage of activated H-Ras in EJ cells and inhibits their growth. We report here on structural elements in S-prenyl derivatives that specifically inhibit the growth of EJ cells, but not of untransformed Rat-1 cells. Inhibition of the Ras-dependent extracellular signal-regulated protein kinase (ERK), of DNA synthesis and of EJ cell growth were apparent after treatment with FTS or its 5-fluoro, 5-chloro and 4-fluoro derivatives or with the C20 S-geranylgeranyl derivative of thiosalicylic acid. The 4-Cl-FTS analogue was a weak inhibitor of EJ cell growth. The 3-Cl-FTS analogue and the FTS carboxyl methyl ester were inactive, as were the C10 S-geranyl derivative of thiosalicylic acid, farnesoic acid, N-acetyl-S-farnesyl-L-cysteine and S-farne-sylthiopropionic acid. The structural requirements for anti-Ras activity of S-prenyl analogues thus appear to be rather stringent. With regard to chain length, the C15 farnesyl group linked to a rigid backbone seems to be necessary and sufficient. A free carboxyl group in an appropriately rigid orientation, as in thiosalicylic acid, is also required. Halogenic substitutents on the benzene ring of the thiosalicylic acid are tolerated only at position 5 or 4. This information may facilitate the design of potent Ras antagonists and deepen our understanding of the mode of association of Ras with the plasma membrane.

22/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09771630 98263352 PMID: 9600961

HCC-2, a human chemokine: gene structure, expression pattern, and biological activity.

Pardigol A; Forssmann U; Zucht HD; Loetscher P; Schulz-Knappe P; Baggiolini M; Forssmann WG; Magert HJ
Lower Saxony Institute for Peptide Research, D-30625 Hannover, Germany.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May 26 1998, 95 (11) p6308-13, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Cloning and sequencing of the upstream region of the gene of the CC chemokine HCC-1 led to the discovery of an adjacent gene coding for a CC chemokine that was named "HCC-2." The two genes are separated by 12-kbp and reside in a head-to-tail orientation on chromosome 17. At variance with the genes for HCC-1 and other human CC chemokines, which have a three-exon-two-intron structure, the HCC-2 gene consists of four exons and three introns. Expression of HCC-2 and HCC-1 as studied by Northern analysis revealed, in addition to the regular, monocistronic mRNAs, a common, bicistronic transcript. In contrast to HCC-1, which is expressed constitutively in numerous human tissues, HCC-2 is expressed only in the gut and the liver. HCC-2 shares significant sequence homology with CKbeta8 and the murine chemokines C10 , CCF18/MRP-2, and macrophage inflammatory protein 1gamma, which all contain six instead of four conserved cysteines. The two additional cysteines of HCC-2 form

a third disulfide bond, which anchors the COOH-terminal domain to the core of the molecule. Highly purified recombinant HCC-2 was tested on neutrophils, eosinophils, monocytes, and lymphocytes and was found to exhibit marked functional similarities to macrophage inflammatory protein 1alpha. It is a potent chemoattractant and inducer of enzyme release in monocytes and a moderately active attractant for eosinophils. Desensitization studies indicate that HCC-2 acts mainly via CC chemokine receptor CCR1.

22/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09474273 97459923 PMID: 9311996
Intermediates in the formation of mouse 20S proteasomes: implications for the assembly of precursor beta subunits.
Nandi D; Woodward E; Ginsburg DB; Monaco JJ
Howard Hughes Medical Institute and Department of Molecular Genetics, University of Cincinnati, 231 Bethesda Avenue, Cincinnati, OH 45267-0524, USA.
EMBO journal (ENGLAND) Sep 1 1997, 16 (17) p5363-75, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI33605, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The assembly of individual proteasome subunits into catalytically active mammalian 20S proteasomes is not well understood. Using subunit-specific antibodies, we characterized both precursor and mature proteasome complexes. Antibodies to PSMA4 (C9) immunoprecipitated complexes composed of alpha, precursor beta and processed beta subunits. However, antibodies to PSMA3 (C8) and PSMB9 (LMP2) immunoprecipitated complexes made up of alpha and precursor beta but no processed beta subunits. These complexes possess short half-lives, are enzymatically inactive and their molecular weight is approximately 300 kDa. Radioactivity chases from these complexes into mature, long-lived approximately 700 kDa proteasomes. Therefore, these structures represent precursor proteasomes and are probably made up of two rings: one containing alpha subunits and the other, precursor beta subunits. The assembly of precursor proteasomes occurs in at least two stages, with precursor beta subunits PSMB2 (C7-I), PSMB3 (C10-II), PSMB7 (Z), PSMB9 (LMP2) and PSMB10 (LMP10) being incorporated before others [PSMB1 (C5), PSMB6 (delta), and PSMB8 (LMP7)]. Proteasome maturation (processing of the beta subunits and juxtaposition of the two beta rings) is accompanied by conformational changes in the (outer) alpha rings, and may be inefficient. Finally, interferon-gamma had no significant effect on the half-lives or total amounts of precursor or mature proteasomes.

22/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09227119 97048015 PMID: 8892856
Disulfide bonds of herpes simplex virus type 2 glycoprotein gB.
Norais N; Tang D; Kaur S; Chamberlain SH; Masiarz FR; Burke RL; Marcus F
Chiron Corporation, Emeryville, California 94608, USA.
Journal of virology (UNITED STATES) Nov 1996, 70 (11) p7379-87, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Glycoprotein B (gB) is the most highly conserved envelope glycoprotein of herpesviruses. The gB protein is required for virus infectivity and cell penetration. Recombinant forms of gB being used for the development of subunit vaccines are able to induce virus-neutralizing antibodies and

protective efficacy in animal models. To gain structural information about the protein, we have determined the location of the disulfide bonds of a 696-amino-acid residue truncated, recombinant form of herpes simplex virus type 2 glycoprotein gB (HSV gB2t) produced by expression in Chinese hamster ovary cells. The purified protein, which contains virtually the entire extracellular domain of herpes simplex virus type 2 gB, was digested with trypsin under nonreducing conditions, and peptides were isolated by reversed-phase high-performance liquid chromatography (HPLC). The peptides were characterized by using mass spectrometry and amino acid sequence analysis. The conditions of cleavage (4 M urea, pH 7) induced partial carbamylation of the N termini of the peptides, and each disulfide peptide was found with two or three different HPLC retention times (peptides with and without carbamylation of either one or both N termini). The 10 cysteines of the molecule were found to be involved in disulfide bridges. These bonds were located between Cys-89 (C1) and Cys-548 (C8), Cys-106 (C2) and Cys-504 (C7), Cys-180 (C3) and Cys-244 (C4), Cys-337 (C5) and Cys-385 (C6), and Cys-571 (C9) and Cys-608 (C10). These disulfide bonds are anticipated to be similar in the corresponding gBs from other herpesviruses because the 10 cysteines listed above are always conserved in the corresponding protein sequences.

22/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09185525 96285596 PMID: 8689632
Altered glutathione metabolism in oxaliplatin resistant ovarian carcinoma cells.
el-akawi Z; Abu-hadid M; Perez R; Glavy J; Zdanowicz J; Creaven PJ; Pendyala L
Department of Investigational Therapeutics, Roswell Park Cancer Institute, Buffalo, NY 14263, USA.
Cancer letters (IRELAND) Jul 19 1996, 105 (1) p5-14, ISSN 0304-3835 Journal Code: CMX
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Elevation of glutathione (GSH) is commonly observed in cellular resistance to a number of anticancer agents. Most frequently reported change in GSH metabolism that is associated with the elevated GSH levels is increased mRNA expression and activity of gamma-glutamyl cysteine synthetase (gamma GCS), the first enzyme of the GSH biosynthetic pathway. We have isolated sublines of the A2780 ovarian carcinoma cell line (C10 and C25) that are 8- and 12-fold resistant to oxaliplatin by repeatedly exposing the cells to increasing concentrations of the platinum agent. The GSH levels in C10 and C25 cell sublines are 3.1- and 3.8-fold higher than the parent A2780 cell line. The mRNA levels and activities for gamma GCS and that for gamma-glutamyl transpeptidase (gamma GT), the GSH salvage pathway enzyme, were measured in these cells. The mRNA for gamma GT and gamma GCS were measured by RT-PCR, with quantitation of the PCR product by HPLC; mRNA levels are expressed as ratios to beta-actin mRNA, used as an endogenous standard. GSH and gamma GCS activity were measured by HPLC assays and gamma GT activity by a colorimetric assay. The increase in GSH in C10 and C25 was associated with an elevation in gamma GT mRNA (2.5- and 8-fold) and gamma GT activity (2.7- and 2.8-fold). No changes were observed in gamma GCS mRNA levels or activity. The data indicate that alterations in GSH metabolism leading to elevations in cellular GSH in A2780 ovarian carcinoma cells selected for low levels of resistance to oxaliplatin are mediated by gamma GT, the "salvage' pathway, rather than an increase in GSH biosynthesis.

22/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09125158 97087136 PMID: 8933154
Leukocyte migration and activation by murine chemokines.
Haelens A; Wuyts A; Proost P; Struyf S; Opdenakker G; van Damme J
Rega Institute for Medical Research, University of Leuven, Laboratory for Molecular Immunology, Belgium.
Immunobiology (GERMANY) Oct 1996, 195 (4-5) p499-521, ISSN 0171-2985 Journal Code: GH3
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Chemokines are a family of chemotactic cytokines which attract different types of leukocytes. This property, combined with some additional inflammatory and growth-regulatory activities, demonstrate their crucial role in the immune system. Chemokines are low molecular weight proteins and possess a typical positioning of four conserved cysteines. This family is further subdivided in two subfamilies depending on whether the first two cysteines are adjacent or not (CC and CXC chemokines, respectively). The CXC chemokines (including interleukin-8) predominantly attract neutrophils, whereas CC chemokines induce migration of monocytes, as well as other leukocyte cell types. In this article, the general characteristics of chemokines are reviewed. Furthermore, the murine CC chemokines, JE/MCP-1, MCP-3/MARC, MIP-1 alpha, MIP-1 beta, RANTES, TCA3, C10/MRP-1, MRP-2, and eotaxin, are discussed more in detail.

22/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09102560 97122438 PMID: 8968058
Inhibition of rat liver cytochrome P450 isozymes by isothiocyanates and their conjugates: a structure-activity relationship study.
Conaway CC; Jiao D; Chung FL
Division of Carcinogenesis and Molecular Epidemiology, American Health Foundation, Valhalla, New York 10595, USA.
Carcinogenesis (ENGLAND) Nov 1996, 17 (11) p2423-7, ISSN 0143-3334 Journal Code: C9T
Contract/Grant No.: CA46535, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A series of arylalkyl and alkyl isothiocyanates, and their glutathione, cysteine , and N-acetylcysteine conjugates were used to study their inhibitory activity toward the dealkylation of ethoxyresorufin (EROD), pentoxyresorufin (PROD), and methoxyresorufin (MROD) in liver microsomes obtained from the 3-methylcholanthrene or phenobarbital-treated rats. These reactions are predominantly mediated by cytochrome P450 (P450) isozymes 1A1 and 1A2, 2B1 and 1A2, respectively. All isothiocyanates inhibited PROD more readily than EROD. Increases in the alkyl chain length of arylalkyl isothiocyanates to C6 resulted in an increased inhibitory potency in these assays; at longer alkyl chain lengths (C8-C10) the inhibitory potency declined. The IC50s for phenethyl isothiocyanate (PEITC) were 47, 46 and 1.8 microM for EROD, MROD and PROD, respectively. Substitution of an additional phenyl group on PEITC also increased the inhibitory potency; the IC50s for 1,2-diphenylethyl isothiocyanate (1,2-DPEITC) and 2,2-diphenylethyl isothiocyanate (2,2-DPEITC) were 0.9 and 0.26 microM for EROD, and 0.045 and 0.13 microM for PROD, respectively. The relative inhibitory potency of PEITC and its conjugates was N-acetylcysteine-PEITC (PEITC-NAC) < glutathione-PEITC (PEITC-GSH) < cysteine -PEITC (PEITC-CYS) < PEITC. The observations that the parent isothiocyanates were more potent inhibitors than the conjugates suggest that dissociation of the conjugate is required for activity. Naturally occurring alkyl isothiocyanates, sulforaphane (SFO) and allyl isothiocyanate (AITC), were very weak inhibitors in the assays. These results suggest the potential of

isothiocyanates as structural probes for studying P450 isozymes. In addition, the inhibitory activity of isothiocyanates for PROD correlated with the previously demonstrated tumor inhibitory potency in (4-methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) induced A/J mouse lung tumor bioassays, which supports earlier findings that P450 2B1 is one of the major isozymes involved in NNK activation and that inhibition of this isozyme is an important mechanism for the chemopreventive activity of isothiocyanates.

22/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08916070 96217603 PMID: 8636420
Farnesyl analogues inhibit vasoconstriction in animal and human arteries.
Roullet JB; Xue H; Chapman J; McDougal P; Roullet CM; McCarron DA
Department of Nephrology, Hypertension and Clinical Pharmacology, Oregon Health Sciences University, Portland 97201, USA.
Journal of clinical investigation (UNITED STATES) May 15 1996, 97 (10) p2384-90, ISSN 0021-9738 Journal Code: HS7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Recent studies have suggested that nonsterol, mevalonate-derived metabolites are implicated in the control of vascular tone and blood pressure. Because of the metabolic importance of farnesyl pyrophosphate, a 15-carbon (C15) intermediate of the cholesterol pathway, the vasoactive properties of the farnesyl motif were investigated. Two farnesyl analogues were used: farnesol, the natural dephosphorylated form of farnesyl pyrophosphate, and N-acetyl-S-trans,trans-farnesyl-L-cysteine (AFC), a synthetic mimic of the carboxyl terminus of farnesylated proteins. Both compounds inhibited NE-induced vasoconstriction in rat aortic rings at micromolar concentration. Their action was rapid, dose dependent, and reversible. Shorter (C10) and longer (C20) isoprenols as well as N-acetyl-S-geranyl-L-cysteine (C10) did not inhibit the response to NE. In contrast, N-acetyl-S-geranylgeranyl-L-cysteine (C20), exhibited vasoactive properties similar to AFC. It was further demonstrated that AFC and farnesol inhibited KCl and NaF-induced contractions, suggesting a complex action on Ca2+ channels and G protein-dependent pathways. Finally, the effect of farnesol and AFC on the NE response was reproduced in human resistance arteries. In conclusion, mevalonate-derived farnesyl analogues are potent inhibitors of vasoconstriction. The study suggests that farnesyl cellular availability is an important determinant of vascular tone in animals and humans, and provides a basis for exploring farnesyl metabolism in humans with compromised vascular function as well as for using farnesyl analogues as regulators of arterial tone in vivo.

22/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08885539 95062229 PMID: 7972030
The palmitoylated cysteine of the cytoplasmic tail of alpha 2A-adrenergic receptors confers subtype-specific agonist-promoted downregulation.
Eason MG; Jacinto MT; Theiss CT; Liggett SB
Department of Medicine (Pulmonary), University of Cincinnati College of Medicine, OH 45267-0564.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov 8 1994, 91 (23) p11178-82, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
Most guanine nucleotide binding protein (G protein)-coupled receptors have a conserved cysteine in the C-terminal cytoplasmic tail near the seventh transmembrane spanning region. This cysteine is known to be palmitoylated in rhodopsin, the beta 2-adrenergic receptor (beta 2AR) and the alpha 2A-adrenergic receptor (alpha 2AAR). For the beta 2AR, this cysteine has been shown to be important for stimulatory G protein (Gs) coupling and agonist-promoted desensitization. For the alpha 2AAR (human alpha 2 C10) palmitoylation occurs at Cys-442, but it is not known what function such fatty acid acylation subserves. The closely related alpha 2CAR subtype denoted alpha 2C4 lacks a cysteine in this region and has different G-protein-coupling characteristics and agonist regulatory properties as compared to alpha 2C10. To assess the role of the palmitoylcysteine in alpha 2AR function, we constructed a mutated alpha 2C10 having a phenylalanine (the analogous amino acid in the alpha 2C4 in this position) substituted for Cys-442, denoted alpha 2C10(Phe-442), and expressed this along with wild-type alpha 2C10 and alpha 2C4 in CHO cells. Functional coupling to inhibitory G protein (Gi) and to Gs was identical between wild-type alpha 2C10 and alpha 2C10(Phe-442). Agonist-promoted desensitization of both the Gi and Gs-mediated pathways was also found to be unaffected by this mutation. Cellular trafficking induced by agonist exposure was evaluated by delineation of intracellular (sequestered) versus cell surface receptors and by determination of net receptor loss. Mutation of Cys-442 did not alter the extent or rate of agonist-promoted sequestration induced by agonists or the recovery from sequestration. However, the downregulation of receptor number after prolonged agonist exposure was completely abolished by this mutation and converted alpha 2C10 to an alpha 2C4 phenotype in regard to this adaptive response. Another mutated alpha 2C10, in which Cys-442 was replaced by alanine, also failed to downregulate. Thus, the function of this cytoplasmic palmitoylcysteine is distinctly different between the alpha 2AR and other G-protein-coupled receptors such as the beta 2AR and rhodopsin, and this suggests that this molecular attribute may subserve diverse roles among members of this family of receptors. For the alpha 2ARs, this may represent an evolved feature that provides for differing needs for regulation of the alpha 2C10 and alpha 2C4 subtypes by agonist.

22/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08860696 94362567 PMID: 8081261
Trypanosoma cruzi: identification of a membrane cysteine proteinase linked through a GPI anchor.
Fresno M; Hernandez-Munain C; de-Diego J; Rivas L; Scharfstein J; Bonay P
Centro de Biologia Molecular, Universidad Autonoma de Madrid, Spain.
Brazilian journal of medical and biological research (BRAZIL) Feb 1994, 27 (2) p431-7, ISSN 0100-879X Journal Code: BOF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The biochemical and functional properties of T. cruzi GP50/55, a novel glycosylphosphatidylinositol (GPI)-anchored membrane antigen have been investigated. A 50-52-kDa thiol proteinase activity could be immunoprecipitated with monoclonal antibodies (mAb) directed against GP50/55 (mAb C10), different from the one reactive with mAbs against lysosomal cysteine proteinase GP57/51. Furthermore, the mAb C10 -reactive proteinase corresponded to the GPI-anchored surface antigen since the proteolytic and antigenic activity partitioned to the aqueous phase after Triton X114 phase separation of phosphatidylinositol specific phospholipase C (PI-PLC)-treated parasites. Of several proteins immunoprecipitated by a polyclonal anti-lysosomal cysteine proteinase, an mAb to GP57/51 recognized a 60-kDa protein, whereas mAb C10 recognized antigens ranging between 52 and 50 kDa. The GP50/55

antigen detected by mAb C10 is expressed on the parasite surface whereas the GP57/51 antigen is mainly intracellular. The internal peptide sequence obtained from purified GP50/55 showed that it is more homologous to the prototype of the cysteine proteinases superfamily, papain, than to the two T. cruzi lysosomal cysteine proteinases so far described. Our data indicate that the T. cruzi GP50/55 is a novel GPI-anchored cysteine proteinase and may represent another isoform of this heterogeneous group of proteinases.

22/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08123778 94176615 PMID: 8130328
A structural model of the tetrodotoxin and saxitoxin binding site of the Na+ channel.
Lipkind GM; Fozzard HA
Cardiac Electrophysiology Laboratories, University of Chicago, Illinois 60637.
Biophysical journal (UNITED STATES) Jan 1994, 66 (1) p1-13, ISSN 0006-3495 Journal Code: A5S
Contract/Grant No.: PO1-HL20592, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Biophysical evidence has placed the binding site for the naturally occurring marine toxins tetrodotoxin (TTX) and saxitoxin (STX) in the external mouth of the Na+ channel ion permeation pathway. We developed a molecular model of the binding pocket for TTX and STX, composed of antiparallel beta-hairpins formed from peptide segments of the four S5-S6 loops of the voltage-gated Na+ channel. For TTX the guanidinium moiety formed salt bridges with three carboxyls, while two toxin hydroxyls (C9-OH and C10 -OH) interacted with a fourth carboxyl on repeats I and II. This alignment also resulted in a hydrophobic interaction with an aromatic ring of phenylalanine or tyrosine residues for the brainII and skeletal Na+ channel isoforms, but not with the cysteine found in the cardiac isoform. In comparison to TTX, there was an additional interaction site for STX through its second guanidinium group with a carboxyl on repeat IV. This model satisfactorily reproduced the effects of mutations in the S5-S6 regions and the differences in affinity by various toxin analogs. However, this model differed in important ways from previously published models for the outer vestibule and the selectivity region of the Na+ channel pore. Removal of the toxins from the pocket formed by the four beta-hairpins revealed a structure resembling a funnel that terminated in a narrowed region suitable as a candidate for the selectivity filter of the channel. This region contained two carboxyls (Asp384 and Glu942) that substituted for molecules of water from the hydrated Na+ ion. Simulation of mutations in this region that have produced Ca2+ permeation of the Na+ channel created a site with three carboxyls (Asp384, Glu942, and Glu1714) in proximity.

22/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08079286 94018366 PMID: 8412494
Molecular determinants of the alpha-2D adrenergic receptor subtype.
Blaxall HS; Heck DA; Bylund DB
Department of Pharmacology, University of Nebraska Medical Center, Omaha 68198-6260.
Life sciences (ENGLAND) 1993, 53 (17) pPL255-9, ISSN 0024-3205 Journal Code: L62
Contract/Grant No.: GM40784, GM, NIGMS
Languages: ENGLISH

Document type: Journal Article
Record type: Completed

The alpha-2 adrenergic receptor in the bovine pineal gland and the rodent homologues of the human alpha-2-C10 receptor express alpha-2D subtype pharmacological characteristics. The alpha-2 adrenergic receptor in the chicken pineal expresses characteristics similar to the alpha-2A subtype found in human and pig. The rodent receptors (alpha-2D) contain a serine residue at position 201 whereas the human and porcine receptors (alpha-2A) have a cysteine at this position. Our results indicate that the bovine pineal receptor has a serine at position 201, supporting the alpha-2D classification. However, the chicken pineal receptor also contains a serine at position 201 suggesting that other amino acids may be responsible for the differences in pharmacological characteristics.

22/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07822392 90375485 PMID: 2398053

Identification of a C-terminal protein carboxyl methyltransferase in rat liver membranes utilizing a synthetic farnesyl cysteine-containing peptide substrate.

Stephenson RC; Clarke S
Department of Chemistry and Biochemistry, University of California, Los Angeles 90024.

Journal of biological chemistry (UNITED STATES) Sep 25 1990, 265 (27) p16248-54, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM-07185, GM, NIGMS; GM-26020, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Polypeptides synthesized in eucaryotic cells with a C-terminal -Cys-Xaa-Xaa-Xaa (-CXXX) sequence are candidates for post-translational modifications that include the removal of the last 3 amino acids and the lipidation and methyl esterification of the cysteinyl residue. To characterize the methylation reaction in vitro, the peptide Leu-Ala-Arg-Tyr-Lys-Cys (LARYKC) and its S-isoprenylated and S-alkylated derivatives were synthesized and assayed as methyl-accepting substrates with subcellular fractions of rat tissues including liver microsomal membranes. While little or no peptide-specific methyltransferase activity was detected in the latter preparation using the unmodified hexapeptide, the C10, C15, and C20 isoprenylated derivatives were substrates with Km values of 389 microM for S-geranyl-LARYKC, 2.2 microM for S-farnesyl-LARYKC, and approximately 10.9 microM for S-geranylgeranyl-LARYKC. The methyl-acceptor activities of a variety of n-alkyl S-derivatives of LARYKC (C8, C10, C13, C15) were also tested; all of these compounds were poorer substrates than the S-geranyl derivative. This enzyme activity uses S-adenosyl-L-methionine as the methyl donor (Km = 2.1 microM) and can be inhibited by S-adenosylhomocysteine (Ki = 9.2 microM), a product of the methylation reaction. The S-farnesyl-LARYKC peptide can inhibit the carboxyl methylation of bovine retinal rod outer segment membrane proteins that was previously shown to occur at the alpha-carboxyl group of C-terminal cysteine residues, demonstrating that the same enzyme can methylate both peptides and proteins. These results suggest that the methyl esterification of proteins containing a C-terminal -CXXX sequence requires not only the removal of the 3 terminal amino acids, but the isoprenylation of the sulfhydryl group as well.

22/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07771254 91177827 PMID: 1706706

Characterization of the Cephalosporium acremonium pcbAB gene encoding

alpha-aminoadipyl-cysteinyl -valine synthetase, a large multidomain peptide synthetase: linkage to the pcbC gene as a cluster of early cephalosporin biosynthetic genes and evidence of multiple functional domains.

Gutierrez S; Diez B; Montenegro E; Martin JF
Department of Ecology, Genetics and Microbiology, University of Leon, Spain.

Journal of bacteriology (UNITED STATES) Apr 1991, 173 (7) p2354-65, ISSN 0021-9193 Journal Code: HH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A 24-kb region of Cephalosporium acremonium C10 DNA was cloned by hybridization with the pcbAB and pcbC genes of Penicillium chrysogenum. A 3.2-kb BamHI fragment of this region complemented the mutation in the structural pcbC gene of the C. acremonium N2 mutant, resulting in cephalosporin production. A functional alpha-aminoadipyl-cysteinyl -valine (ACV) synthetase was encoded by a 15.6-kb EcoRI-BamHI DNA fragment, as shown by complementation of an ACV synthetase-deficient mutant of P. chrysogenum. Two transcripts of 1.15 and 11.4 kb were found by Northern (RNA blot) hybridization with probes internal to the pcbC and pcbAB genes, respectively. An open reading frame of 11,136 bp was located upstream of the pcbC gene that matched the 11.4-kb transcript initiation and termination regions. It encoded a protein of 3,712 amino acids with a deduced Mr of 414,791. The nucleotide sequence of the gene showed 62.9% similarity to the pcbAB gene encoding the ACV synthetase of P. chrysogenum; 54.9% of the amino acids were identical in both ACV synthetases. Three highly repetitive regions occur in the deduced amino acid sequence of C. acremonium ACV synthetase. Each is similar to the three repetitive domains in the deduced sequence of P. chrysogenum ACV synthetase and also to the amino acid sequence of gramicidin synthetase I and tyrocidine synthetase I of Bacillus brevis. These regions probably correspond to amino acid activating domains in the ACV synthetase protein. In addition, a thioesterase domain was present in the ACV synthetases of both fungi. A similarity has been found between the domains existing in multienzyme nonribosomal peptide synthetases and polyketide and fatty acid synthetases. The pcbAB gene is linked to the pcbC gene, forming a cluster of early cephalosporin-biosynthetic genes.

22/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07100673 94030619 PMID: 8216854

The gene for C10, a member of the beta-chemokine family, is located on mouse chromosome 11 and contains a novel second exon not found in other chemokines.

Berger MS; Kozak CA; Gabriel A; Prystowsky MB
Hematology-Oncology Division, Hospital of the University of Pennsylvania, Philadelphia 19104.

DNA and cell biology (UNITED STATES) Nov 1993, 12 (9) p839-47, ISSN 1044-5498 Journal Code: AF9
Contract/Grant No.: CA48648, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

C10 is a recently described member of the beta-chemokine subfamily of the chemokine superfamily of cytokine proteins. Genomic clones encoding murine C10 were isolated and sequenced. The other members of the beta-chemokine family have a three-exon genomic structure containing, among other sequence similarities, four cysteines spaced in a highly conserved manner. In each of these genes, the second exon contains the first three of the four conserved cysteines, and the third exon contains the last. In contrast to this genomic structure, the C10

gene has four exons, with a novel second exon of 48 nucleotides. Exons 3 and 4 of C10 contain four cysteines distributed in the same manner as in exons 2 and 3 of other beta-chemokine family members. The novel second exon codes for a large number of charged amino acids, and this exon shows no homology to any previously described sequences in computer databases. Linkage studies showed that the C10 gene (Scya6) is closely linked to the Scya2 locus on mouse chromosome 11, indicating that the C10 gene is located in the same region of mouse chromosome 11 as other members of the beta-chemokine family. Thus, although the C10 gene contains a novel exon not found in any other members of the chemokine superfamily, its chromosomal location and conservation of cysteine residues and other structural features suggest that it evolved from the same ancestral gene as other members of the beta-chemokine family.

22/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05614126 89011662 PMID: 3050069
A synthetic luteinizing hormone releasing hormone vaccine. I. Conjugation and specificity trials in BALB/c mice.
Silversides DW; Allen AF; Misra V; Qualtiere L; Mapletoft RJ; Murphy BD
Department of Veterinary Physiology, University of Saskatchewan, Saskatoon, Canada.
Journal of reproductive immunology (NETHERLANDS) Aug 1988, 13 (3) p249-61, ISSN 0165-0378 Journal Code: JWS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The immunobiology of luteinizing hormone releasing hormone (LHRH) was explored, to provide a conceptual and practical basis for the use of LHRH in immunocastration. Cysteine substituted analogues of LHRH were synthesized including Cys1-LHRH (C1-LHRH), Cys6-LHRH (C6-LHRH) and Cys10-LHRH (C10-LHRH). These were reacted to carrier molecules using the heterobifunctional cross-linking reagent m-maleimidobenzoylsulfosuccinimide ester (SMBS), producing peptide-carrier conjugates of known peptide content and conjugation orientation. This reaction regime was found to be rapid, efficient and allowed for easy control of peptide to carrier ratios. Conjugates were used in active immunization trials in BALB/c mice to characterize the murine immune response against LHRH. BALB/c mice were shown to have the capacity to recognise all three cysteine substituted LHRH analogues and to produce antibodies cross-reactive with native LHRH. The specificity of LHRH antisera generated was found to be dependent on the site of conjugation of the peptide to carrier molecule. C1-LHRH generated carboxy terminal directed antibodies, C10-LHRH generated amino terminal directed antibodies, while C6-LHRH could generate amino terminal directed or carboxy terminal directed antibodies, or both within a given animal. No intrinsically immunodominant epitopes were seen within the LHRH molecule.

22/3,AB/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02894386 76197742 PMID: 1273036
A single column packing for the gas-liquid chromatographic separation of various biologically important compounds.
Schmid K; Chen LC
Preparative biochemistry (UNITED STATES) 1976, 6 (1) p27-56, ISSN 0032-7484 Journal Code: PL5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The use of a single, commercially available column packing, TabsorbR, is

described for the g.l.c. separation of a large number of different compounds. The resolution of the homologous members of the following series of compounds was achieved: (1) saturated fatty acids (C1-C18), (2) normal aliphatic saturated dicarboxylic acids (C2-C14), (3) normal aliphatic saturated alcohols (C1-C24), (4) normal aliphatic saturated amines (C1-C12), (5) the common amino acids except arginine, histidine and cysteine, (6) aliphatic hydrocarbons (C10 -C20) and (7) monosaccharides. It should be noted that twenty-two monosaccharides including three hexosamines and two anhydrohexoses, could be resolved as alditol acetates in a single run. In addition, galacturonic, glucuronic and iduronic acids could be separated from one another as their 1,4-lactones. The resolution achieved in these series of compounds was found to be consistent and highly reproducible. It is of further interest that certain isomers of the higher fatty acids and hydrocarbons with one double bond could also be separated from the normal and saturated compounds, respectively. The applicability of "Tabsorb" for the g.l.c. separation, although noted above to be considerably broad, is by far not yet exhausted. These procedures which form the basis for the quantitative determinations of the various compounds studied as demonstrated by analysis of glycopeptides for neutral hexoses and proteins for the amino acids, can readily be adapted to preparative methods. From the biochemical point of view "Tabsorb" is an extremely versatile column packing in that it can be used for the identification of many of the common building blocks of natural products.

22/3,AB/29 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13275938 BIOSIS NO.: 200100483087
Cytokine-induced activation of nuclear factor-kappaB is inhibited by hydrogen peroxide through oxidative inactivation of IkappaB kinase.
AUTHOR: Korn Solange H; Wouters Emiel F M; Vos Nanda; Janssen-Heininger Yvonne M W(a)
AUTHOR ADDRESS: (a)Dept. of Pathology, University of Vermont, Medical Alumni Bldg., A143, Burlington, VT, 05405: yjanssen@zoo.uvm.edu**USA
JOURNAL: Journal of Biological Chemistry 276 (38):p35693-35700 September 21, 2001
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Rapid activation of the IkappaB kinase (IKK) complex is considered an obligatory step in the activation of nuclear factor-kappaB (NF-kappaB) in response to diverse stimuli. Since oxidants have been implicated in the regulation of NF-kappaB, the focus of the present study was the activation of IKK by tumor necrosis factor alpha (TNFalpha) in the presence or absence of hydrogen peroxide (H2O2). Exposure of mouse alveolar epithelial cells to H2O2 was not sufficient to activate IKK, degrade IkappaBalpha, or activate NF-kappaB. In contrast, TNFalpha induced IKK activity rapidly and transiently resulting in IkappaBalpha degradation and NF-kappaB activation. Importantly, in the presence of H2O2, the ability of TNFalpha to induce IKK activity was markedly decreased and resulted in prevention of IkappaBalpha degradation and NF-kappaB activation. Neither tyrosine kinases nor phosphatidylinositol 3-kinases, known regulators of NF-kappaB by oxidants, were involved in IKK inhibition by H2O2. Direct addition of H2O2 to the immunoprecipitated IKK complex inhibited enzyme activity. Inhibition of IKK activity by H2O2 was associated with direct oxidation of cysteine residues present in the IKK complex and occurred only in enzymatically active IKK. In

contrast to previously published observations, our findings demonstrate that the oxidant H2O2 reduces NF-kappaB activation by inhibiting activated IKK activity.

2001

22/3,AB/30 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13265775 BIOSIS NO.: 200100472924
Chemically modified enzymes.
AUTHOR: Bott Richard R; Graycar Thomas P; Jones J Bryan(a); Mitchinson Colin
AUTHOR ADDRESS: (a)1275 Seaforth Crescent, Lakefield**Canada
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1249 (3):pNo Pagination Aug. 21, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Modified enzymes are provided in which at least one amino acid, such as asparagine, leucine, methionine or serine, of an enzyme is replaced with a cysteine and the thiol hydrogen is replaced with a substituent group providing a thiol side chain selected from the group consisting of: a) --SR1 R2, wherein R1 is an alkyl and R2 is a charged or polar moiety; b) --SR3, wherein R3 is a substituted or unsubstituted phenyl; c) --SR4, wherein R4 is substituted or unsubstituted cyclohexyl; d) --SR5, wherein R5 is C10 -C15 alkyl; and e) --SR6 wherein R6 is a C1-6 alkyl. Also, methods of producing the modified enzymes are provided, as well as detergent and feed additives and a composition for the treatment of a textile. A method for using the modified enzymes in organic synthesis is additionally provided. Further, modified enzymes having improved activity, altered pH profile and/or wash performance are provided.

2001

22/3,AB/31 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13082823 BIOSIS NO.: 200100289972
The preferred stoichiometry of c subunits in the rotary motor sector of Escherichia coli ATP synthase is 10.
AUTHOR: Jiang Weiping; Hermolin Joe; Fillingame Robert H(a)
AUTHOR ADDRESS: (a)Department of Biomolecular Chemistry, University of Wisconsin Medical School, 1300 University Avenue, Madison, WI, 53706: rhfillin@facstaff.wisc.edu**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 98 (9):p4966-4971 April 24, 2001
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The stoichiometry of c subunits in the H+-transporting Fo rotary motor of ATP synthase is uncertain, the most recent suggestions varying

from 10 to 14. The stoichiometry will determine the number of H+ transported per ATP synthesized and will directly relate to the P/O ratio of oxidative phosphorylation. The experiments described here show that the number of c subunits in functional complexes of FoF1 ATP synthase from Escherichia coli can be manipulated, but that the preferred number is 10. Mixtures of genetically fused cysteine-substituted trimers (c3) and tetramers (c4) of subunit c were coexpressed and the c subunits crosslinked in the plasma membrane. Prominent products corresponding to oligomers of c7 and c10 were observed in the membrane and purified FoF1 complex, indicating that the c10 oligomer formed naturally. Oligomers larger than c10 were also observed in the membrane fraction of cells expressing c3 or c4 individually, or in cells coexpressing c3 and c4 together, but these larger oligomers did not copurify with the functional FoF1 complex and were concluded to be aberrant products of assembly in the membrane.

2001

22/3,AB/32 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11851586 BIOSIS NO.: 199900097695
Overexpression, purification, and characterization of human m-calpain and its active site mutant, m-C10-5S-calpain, using a baculovirus expression system.
AUTHOR: Masumoto Hajime(a); Yoshizawa Toshio; Soriamachi Hiroyuki; Nishino Takeshi; Ishiura Shoichi; Suziki Koichi
AUTHOR ADDRESS: (a)Lab. Mol. Structure Function, Inst. Mol. Cell. Biosic., Univ. Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tok**Japan
JOURNAL: Journal of Biochemistry (Tokyo) 124 (5):p957-961 Nov., 1998
ISSN: 0021-924X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recombinant human m-calpain was produced in a soluble form at a level of 20 mg/liter of Sf-9 cell culture by the coexpression of recombinant human m-calpain large (m80K) and small (30K) subunits using a baculovirus expression system. The expressed m-calpain was purified by sequential column chromatographies on DEAE-Toyopearl, gel-filtration, and Mono Q by the same method used to purify native m-calpain. The recombinant m-calpain had a specific activity of 691 U/mg and a Ka value (Ca2+ requirement for 50% caseinolysis activity) of 0.4 mM, which are essentially identical to those of native rabbit m-calpain. A mutant m-calpain large subunit, m-C105S-80K, where the active-site cysteine-105 is converted to serine by site-directed mutagenesis, was coexpressed with 30K in Sf-9 cells, purified, and characterized. m-C105S-calpain does not degrade casein nor an artificial tetra-peptide substrate, succinyl-Leu-Leu-Val-Tyr-MCA. Further, it shows no autolytic activity with Ca2+. This is the first report of the large-scale production of a fully active m-calpain species in the baculovirus system.

1998

22/3,AB/33 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07590056 BIOSIS NO.: 000091118845
CHARACTERIZATION OF THE CEPHALOSPORIUM-ACREMONIUM PCB-AB GENE ENCODING ALPHA AMINOADIPYLCYSTEINYLVALINE SYNTHETASE A LARGE MULTIDOMAIN PEPTIDE

SYNTHETASE LINKAGE TO THE PCB-C GENE AS A CLUSTER OF EARLY CEPHALOSPORIN BIOSYNTHETIC GENES AND EVIDENCE OF MULTIPLE FUNCTIONAL DOMAINS
AUTHOR: GUTIERREZ S; DIEZ B; MONTENEGRO E; MARTIN J F
AUTHOR ADDRESS: SECT. MICROBIOL., DEP. ECOL. GENETICS MICROBIOL., UNIV. LEON, 24071 LEON, SPAIN.
JOURNAL: J BACTERIOL 173 (7). 1991. 2354-2364. 1991
FULL JOURNAL NAME: Journal of Bacteriology
CODEN: JOBAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A 24-kb region of Cephalosporium acremonium C10 DNA was cloned by hybridization with the pcbAB and pcbC genes of Penicillium chrysogenum. A 3.2-kb BamHI fragment of this region complemented the mutation in the structural pcbC gene of the C. acremonium N2 mutant, resulting in cephalosporin production. A functional .alpha.-aminoadipyl-cysteinyl-valine (ACV) synthetase was encoded by a 15.6-kb EcoRI-BamHI DNA fragment, as shown by complementation of an ACV synthetase-deficient mutant of P. chrysogenum. Two transcripts of 1.15 and 11.4 kb were found by Northern (RNA blot) hybridization with probes internal to the pcbC and pcbAB genes, respectively. An open reading frame of 11,136 bp was located upstream of the pcbC gene that matched the 11.4-kb transcript initiation and termination regions. It encoded a protein of 3,712 amino acids with a deduced Mr of 414,791. The nucleotide sequence of the gene showed 62.9% similarity to the pcbAB gene encoding the ACV synthetase of P. chrysogenum; 54.9% of the amino acids were identical in both ACV synthetases. Three highly repetitive regions occur in the deduced amino acid sequence of C. acremonium ACV synthetase. Each is similar to the three repetitive domains in the deduced sequence of P. chrysogenum ACV synthetase and also to the amino acid sequence of gramicidin synthetase I and tyrocidine synthetate I of Bacillus brevis. These regions probably correspond to amino acid activating domains in the ACV synthetase protein. In addition, a thioesterase domain was present in the ACV synthetases of both fungi. A similarity has been found between the domains existing in multienzyme nonribosomal peptide synthetases and polyketide and fatty acid synthetases. The pcbAB gene is linked to the pcbC gene, forming a cluster of early cephalosporin-biosynthetic genes.

1991

22/3,AB/34 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07353739 BIOSIS NO.: 000090132644
IDENTIFICATION OF A CARBOXY-TERMINAL PROTEIN CARBOXYL METHYLTRANSFERASE IN RAT LIVER MEMBRANES UTILIZING A SYNTHETIC FARNESYL CYSTEINE -CONTAINING PEPTIDE SUBSTRATE
AUTHOR: STEPHENSON R C; CLARKE S
AUTHOR ADDRESS: DEP. CHEM. AND BIOCHEM., UNIV. OF CALIFORNIA, LOS ANGELES, CALIF. 90024.
JOURNAL: J BIOL CHEM 265 (27). 1990. 16248-16254. 1990
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Polypeptides synthesized in eucaryotic cells with a C-terminal -Cys-Xaa-Xaa-Xaa (-CXXX) sequence are candidates for post-translational modifications that include the removal of the last 3 amino acids and the lipidation and methyl esterification of the cysteinyl residue. To characterize the methylation reaction in vitro, the peptide Leu-Ala-Arg-Try-Lys-Cys (LA-RYKC) and its S-isoprenylated and S-alkylated

derivatives were synthesized and assayed as methyl-accepting substrates with subcellular fractions of rat tissues including liver microsomal membranes. While little or no peptide-specific methyltransferase activity was detected in the latter preparation using the unmodified hexapeptide, the C1, C15, and C20 isopyrenylated derivatives were substrates with Km values of 389 .mu.M for S-geranyl-LARYKC, 2.2 .mu.M for S-farnesyl-LARYKC, and approximately 10.9 .mu.M for S-geranylgernayl-LA-RYKC. The methyl-acceptor activities of a variety of n-akylk S-derivatives of LARYKC (C8, C10, C13, C15) were also tested; all of these compounds were poorer substrates than the S-geranuyl derivative. This enzyme activity uses S-adenosyl-L-methionine as the methyl donor (Km = 2.1 .mu.M) and can be inhibited by S-adenosylhomocysteine (Ki = 9.2 .mu.M), a product of the methylation reaction. The S-farneysl-LARYKC peptide can inhibit the carboxyl methylation of bovine retinal rod outer segment membrane proteins that was previously shown to occur at the .alpha.-carboxyl group of C-terminal cysteine residues, demonstrating that the same enzyme can methylate both peptides and proteins. These results suggest that the methyl esterfication of proteins containing a C-terminal -CXXX sequence requires not only the removal of the 3 terminal amino acids, but the isoprenylation of the sulfhydryl group as well.

1990

22/3,AB/35 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06817273 BIOSIS NO.: 000088126718
IMMUNIZATION OF CATTLE AGAINST MODIFIED PEPTIDES OF GONADOTROPIN RELEASING HORMONE CONJUGATED TO CARRIERS EFFECTIVENESS OF FREUND'S AND ALTERNATIVE ADJUVANTS
AUTHOR: GOUBAU S; SILVERSIDES D W; GONZALEZ A; LAARVELD B; MAPLETOFT R J; MURPHY B D
AUTHOR ADDRESS: OBSTETRICS AND GYNECOLOGY, UNIV. SASKATCHEWAN, SASKATOON, SASKATCHEWAN, CANADA S7N OWO.
JOURNAL: THERIOGENOLOGY 32 (4). 1989. 557-568. 1989
FULL JOURNAL NAME: Theriogenology
CODEN: THGNB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Two gonadotropin-releasing hormone (GnRH) peptides with a cysteine substitution of the first (C1-GnRH) or tenth (C10 -GnRH) amino acid were conjugated to ovalbumin and equine serum albumin, respectively, via the sulfhydryl group of the introduced cysteine. Animals were immunized three times at 3-wk intervals with both conjugates in either saline (n = 5), Freund's complete adjuvant (FCA; n = 5), Havlogen (n = 6), Ribi adjuvant system (RAS; n = 5), dimethyl dioctadecyl ammonium bromide (DDA; n = 4), Alhydrogel (n = 5) or Regressin (n = 5). Animals immunized with conjugates in saline or RAS did not produce anti-GnRH titers. The highest anti-GnRH titers were produced by animals treated with FCA. The Alhydrogel and DDA treatments stimulated the production of GnRH antibodies in all animals treated, but titers were lower than in animals immunized with FCA. When vaccines were formulated with Havlogen or Regressin, anti-GnRH titers were low or absent. Serum luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels were depressed in FCA and in Alhydrogel treated animals. The antisera raised were predominantly directed against either the carboxy- or the amino-terminal end of the GnRH peptide, or directed equally against both, depending on the individual animal. Results suggest that no epitope of GnRH dominates the immune response in cattle and show that the best alternative to FCA is Alhydrogel.

1989

22/3,AB/36 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06269052 BIOSIS NO.: 000086103235
A SYNTHETIC LHRH I. CONJUGATION AND SPECIFICITY TRIALS IN BALB-C MICE
AUTHOR: SILVERSIDES D W; ALLEN A F; MISRA V; QUALTIER L; MAPLETOFT R J; MURPHY B D
AUTHOR ADDRESS: OBSTET. GYNECOL., UNIV. SASKATCHEWAN, SASKATOON, SASKATCHEWAN S7N 0W0.
JOURNAL: J REPROD IMMUNOL 13 (3). 1987. 249-262. 1987
FULL JOURNAL NAME: Journal of Reproductive Immunology
CODEN: JRIMD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The immunobiology of luteinizing hormone releasing hormone (LHRH) was explored, to provide a conceptual and practical basis for the use of LHRH in immunocastration. Cysteine substituted analogues of LHRH were synthesized including Cys1-LHRH (C1-LHRH), Cys6-LHRH (C6-LHRH) and Cys10-LHRH (C10-LHRH). These were reacted to carrier molecules using the heterobifunctional cross-linking reagent m-maleimidobenzoylsulfosuccinimide ester (SMBS), producing peptide-carrier conjugates of known peptide content and conjugation orientation. This reaction regime was found to be rapid, efficient and allowed for easy control of peptide to carrier ratios. Conjugates were used in active immunization trials in BALB/c mice to characterize the murine immune response against LHRH. BALB/c mice were shown to have the capacity to recognise all three cysteine substituted LHRH analogues and to produce antibodies cross-reactive with native LHRH. The specificity of LHRH antisera generated was found to be dependent on the site of conjugation of the peptide to carrier molecule. C1-LHRH generated carboxy terminal directed antibodies, C10-LHRH generated amino terminal directed antibodies, while C6-LHRH could generate amino terminal directed or carboxy terminal directed antibodies, or both within a given animal. No intrinsically immunodominant epitopes were seen within the LHRH molecule.

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? s (liposom? or poly?) and (decyl

>>>Unmatched parentheses
? s (liposom? or poly?) and decyl

>>>File 155 processing for POLY? stopped at POLYCYANIDE
>>>File 5 processing for POLY? stopped at POLYCERATOCARPUS
          49833  LIPOSOM?
         483658  POLY?
           1318  DECYL
     S13    151  (LIPOSOM? OR POLY?) AND DECYL
? rd

...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...completed examining records
     S14    120  RD (unique items)
? s s14 and py<1998

Processing
           120  S14
      20863023  PY<1998
     S15    106  S14 AND PY<1998
? t s15/3,ab/all


 15/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10742106   97454296   PMID: 9310371
  Characterization of human endothelin B receptor and mutant receptors
expressed in insect cells.
  Doi T; Hiroaki Y; Arimoto I; Fujiyoshi Y; Okamoto T; Satoh M; Furuichi Y
  International Institute for Advanced Research, Matsushita Electric
Industrial Co., Ltd, Seika, Kyoto, Japan. tomoko@crl.mei.co.jp
  European journal of biochemistry (GERMANY)  Aug 15 1997,  248  (1)
  p139-48,  ISSN 0014-2956  Journal Code: EMZ
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  Endothelin type-B receptor (ET(B)R) forms a stable complex with its
ligand, endothelin-1. To facilitate biochemical and biophysical studies of
human ET(B)R, several ET(B)R mutants carrying a hexahistidine tag sequence
at the N or C terminus were expressed in Sf9 cells and were purified by a
combination of biotinylated endothelin-1-ligand-affinity and
nickel-affinity chromatographies. The ligand-free receptor was purified by
dissociating the ligand x receptor complex with 2 M NaSCN, whereas the
ligand-bound ET(B)R was purified by the use of thiol-sensitive biotinylated
endothelin-1. While the wild-type ET(B)R was expressed at about 100 pmol
125I-endothelin-1-binding activity/mg membrane protein, the deletion of 36
residues from the N-terminus reduced the expressed activity to about 30%.
On the other hand, the lack of glycosylation and the replacement of 2-9
residues in the N-terminal tail resulted in a 20-40% reduction in the
expressed activity. Among the mutant proteins, [H57-H62, G63-G65]ET(B)R,
carrying six His residues in the N-terminal tail, was studied extensively
because it was purified most effectively. Ligand-free [H57-H62,
G63-G65]ET(B)R, purified in digitonin, retained full ligand-binding
activity, while other detergents led to partial denaturation of the
receptor after solubilization or after elution with NaSCN. On the other
hand, ligand-bound [H57-H62, G63-G65]ET(B)R could be purified in various
detergents, such as n-octyl-beta-D-glucopyranoside or n-decyl
-beta-D-maltopyranoside. Ligand-free [H57-H62, G63-G65]ET(B)R reconstituted
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in phospholipid vesicles stimulated the binding of guanosine 5'-3-O-(thio)triphosphate by Gq in the presence of endothelin-1. Ligand-bound [H57-H62, G63-G65]ET(B)R showed similar catalytic activity in nucleotide exchange by Gq. These results indicate that the ligand x receptor complex in a detergent-micellar solution retained the biologically active structure, and that the presence of ligand, endothelin-1, in the receptor molecule reinforces the stable assembly of a helical bundle and therefore the active structure.

15/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09659646 98107320 PMID: 9444867
Early detection of tuberculous meningitis using one step competitive ELISA.
Naidu AK; Gogate A
Department of Microbiology, Lokmanya Tilak Municipal Medical College, Sion, Bombay.
Indian journal of pathology & microbiology (INDIA) Oct 1997, 40 (4) p531-8, ISSN 0377-4929 Journal Code: GKK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A one step competitive Enzyme-Linked Immunosorbent assay (ELISA) method was developed to detect mycobacterial antigen in cerebrospinal fluid (CSF) for the diagnosis of tuberculous meningitis and compared with a standard competitive ELISA method. Indigenously prepared soluble extract of Mycobacterium tuberculosis H37 Rv was used as antigen. The study was conducted using CSF of 230 clinically diagnosed cases of tuberculous meningit is and 208 control subjects. A cutoff value of 0.57 ng/ml by the one step ELISA and 0.5 ng/ml by the standard ELISA method were determined. The specificity of both methods were 100% and positivity was 68.26% and 70.43% respectively. A follow up study was conducted in 63 cases at various interval of time after starting anti-tubercular therapy i.e. at 3 weeks (63 cases), 6 weeks (27 cases) and > or = 4-12 months (13 cases). It was observed that antigen levels decreased gradually, but were much above the cutoff range. Indigenously prepared antigen was compared with antigen prepared in other laboratories and standard molecular weight markers using SDS PAGE (Sodium Do-decyl Sulphate Polycrylamide Gel Electrophoresis).

15/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09506698 95226288 PMID: 7710936
Effect of axial ligation and delivery system on the tumour-localising and -photosensitising properties of Ge(IV)-octabutoxy-phthalocyanines.
Soncin M; Polo L; Reddi E; Jori G; Kenney ME; Cheng G; Rodgers MA
Department of Biology, University of Padova, Italy.
British journal of cancer (SCOTLAND) Apr 1995, 71 (4) p727-32, ISSN 0007-0920 Journal Code: AV4
Contract/Grant No.: CA 46281, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Four Ge(IV)-octabutoxy-phthalocyanines (GePcs) bearing two alkyl-type axial ligands were assayed for their pharmacokinetic properties and phototherapeutic efficiency in Balb/c mice bearing an intramuscularly transplanted MS-2 fibrosarcoma. The GePcs were i.v. injected at a dose of 0.35 mumol kg-1 body weight after incorporation into either Cremophor emulsions or small unilamellar liposomes of dipalmitoyl-phosphatidylc holine (DPPC). Both the nature of the delivery system and the chemical

structure of the phthalocyanine were found to affect the behaviour of the GePcs in vivo. Thus, Cremophor-administered GePcs invariably yielded a more prolonged serum retention and a larger association with low-density lipoproteins (LDLs) as compared with the corresponding liposome -delivered phthalocyanines. This led to a greater efficiency and selectivity of tumour targeting. These effects were more pronounced for those GePcs having relatively long alkyl chains (hexyl to decyl) in the axial ligands. Maximal tumour accumulation (0.67 nmol per g of tissue) was found for Ge-Pc(hexyl)2 at 24 h after injection. Consistently, the Ge-Pc(hexyl)2, administered via Cremophor, showed the highest phototherapeutic activity towards MS-2 fibrosarcoma.

15/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09502297 96078857 PMID: 7586094
Solubilizing effects caused by alkyl pyridinium surfactants in phosphatidylcholine liposomes.
de la Maza A; Parra JL
Departamento de Tensioactivos, Consejo Superior de Investigaciones Cientificas (C.S.I.C.), C/ Jordi Girona, Barcelona, Spain.
Chemistry and physics of lipids (IRELAND) Aug 1 1995, 77 (1) p79-87, ISSN 0009-3084 Journal Code: CZW
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The solubilization of neutral and electrically charged liposomes by a series of alkyl pyridinium surfactants (alkyl chain lengths C10-C14) was investigated. Solubilization was detected as a decrease in static light-scattering of liposome suspensions. Two parameters were regarded as corresponding to the effective surfactant/lipid molar ratios at which the surfactant saturated the liposomes Re(sat) and led to a complete solubilization of these structures Re(sol). From these parameters the corresponding surfactant partition coefficients were determined. The Re and K parameters fell as the surfactant alkyl chain length decreased or both the critical micellar concentration (CMC) and the hydrophilic/lipophilic balance (HLB number) increased, regardless of the bilayers electrical charge. Thus, although decyl-pyridinium bromide (DePB) showed the highest ability for saturation and solubilization of bilayers, its concentration was always higher than that needed for dodecyl-pyridinium bromide (DoPB) and tetradecyl-pyridinium bromide (TePB), the last one being the most active. These results emphasize the influence of the hydrophilic/lipophilic balance of these surfactants on liposome solubilization and the minor influence of the electrostatic factors in this process.

15/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09490303 95100522 PMID: 7802252
Cyclic polyamine ionophore for use in a dibasic phosphate-selective electrode.
Carey CM; Riggan WB
American Dental Association Health Foundation, Paffenbarger Research Center, National Institute of Standards and Technology, Gaithersburg, Maryland 20899.
Analytical chemistry (UNITED STATES) Nov 1 1994, 66 (21) p3587-91, ISSN 0003-2700 Journal Code: 4NR
Contract/Grant No.: DE10851, DE, NIDCR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A cyclic polyamine, 3-decyl-1,5,8-triazacyclodecane-2,4-dione (N3-cyclic amine), was used as the ionophore for a dibasic phosphate-selective electrode. This electrode exhibited a linear response between 1.0 mumol/L and 0.1 mol/L dibasic phosphate activity with a near-Nernstian slope of approximately -29 mV per activity decade. The electrode selectivity for dibasic phosphate over other commonly occurring anions was evaluated. A mechanism for the selectivity of the electrode toward HOP4(2-) ions is postulated to be a function of the size and charge of the N3-cyclic amine ionophore relative to the size and charge of HPO4(2-) ions. The electrode's superior selectivity and sensitivity make possible the direct measurement of phosphate activity in a wide variety of applications.

15/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09485780 94327693 PMID: 8051204
Reconstitution of native-type noncrystalline lens fiber gap junctions from isolated hemichannels.
Kistler J; Goldie K; Donaldson P; Engel A
School of Biological Sciences, Center for Gene Technology, University of Auckland, New Zealand.
Journal of cell biology (UNITED STATES) Aug 1994, 126 (4) p1047-58, ISSN 0021-9525 Journal Code: HMV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Gap junctions contain numerous channels that are clustered in apposed membrane patches of adjacent cells. These cell-to-cell channels are formed by pairing of two hemichannels or connexons, and are also referred to as connexon pairs. We have investigated various detergents for their ability to separately solubilize hemichannels or connexon pairs from isolated ovine lens fiber membranes. The solubilized preparations were reconstituted with lipids with the aim to reassemble native-type gap junctions and to provide a model system for the characterization of the molecular interactions involved in this process. While small gap junction structures were obtained under a variety of conditions, large native-type gap junctions were assembled using a novel two-step procedure: in the first step, hemichannels that had been solubilized with octylpolyoxyethylene formed connexon pairs by dialysis against n-decyl -beta-D-maltopyranoside. In the second step, connexon pairs were reconstituted with phosphatidylcholines by dialysis against buffer containing Mg2+. This way, double-layered gap junctions with diameter < or = 300 nm were obtained. Up to several hundred channels were packed in a noncrystalline arrangement, giving these reconstituted gap junctions an appearance that was indistinguishable from that of the gap junctions in the lens fiber membranes.

15/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09379960 97362286 PMID: 9211943
The smallest membrane anchoring subunit (QPs3) of bovine heart mitochondrial succinate-ubiquinone reductase. Cloning, sequencing, topology, and Q-binding domain.
Shenoy SK; Yu L; Yu CA
Department of Biochemistry & Molecular Biology, Oklahoma State University, Stillwater, OK 74078, USA.
Journal of biological chemistry (UNITED STATES) Jul 11 1997, 272 (28) p17867-72, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM30721, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
The cDNA encoding the smallest membrane-anchoring subunit (QPs3) of bovine heart mitochondrial succinate-ubiquinone reductase was cloned and sequenced. This cDNA is 1330 base pairs long with an open reading frame of 474 base pairs that encodes the 103 amino acid residues of mature QPs3 and a 55-amino acid residue presequence. The cDNA insert has an 820-base pair long 3'-untranslated region, including a poly(A) tail. The molecular mass of QPs3, deduced from the nucleotide sequence, is 10,989 Da. QPs3 is a very hydrophobic protein; the hydropathy plot of the amino acid sequence reveals three transmembrane helices. Previous photoaffinity labeling studies of succinate-ubiquinone reductase, using 3-azido-2-methyl-5-methoxy [3H]-6-decyl -1,4-benzoquinone ([3H]azido-Q), identified QPs3 as one of the putative Q-binding proteins in this reductase. An azido-Q-linked peptide with a retention time of 66 min is obtained by high performance liquid chromatography of the chymotrypsin digest of carboxymethylated and succinylated [3H]azido-Q-labeled QPs3 purified from labeled succinate-ubiquinone reductase by a procedure involving phenyl-Sepharose 4B column chromatography, preparative SDS-polyacrylamide gel electrophoresis, and acetone precipitation. The amino acid sequence of this peptide is NH2-L-N-P-C-S-A-M-D-Y-COOH, corresponding to residues 29-37. The structure of QPs3 in the inner mitochondrial membrane is proposed based on the hydropathy profile of the amino acid sequence, on the predicted tendencies to form alpha-helices and beta-sheets, and on immunobinding of Fab' fragmenthorseradish peroxidase conjugates prepared from antibodies against two synthetic peptides, corresponding to the NH2 terminus region and the loop connecting helices 2 and 3 of QPs3, in mitoplasts and submitochondrial particles. The ubiquinone-binding domain in the proposed model of QPs3 is probably located at the end of transmembrane helix 1 toward the C-side of the mitochondrial inner membrane.

15/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09238043 98177736 PMID: 9552311
Development of a transdermal patch of methadone: in vitro evaluation across hairless mouse and human cadaver skin.
Ghosh TK; Bagherian A
Department of Pharmaceutical Sciences, College of Pharmacy and Pharmaceutical Sciences, Howard University, Washington, DC 20059, USA.
Pharmaceutical development and technology (UNITED STATES) Oct 1996, 1 (3) p285-91, ISSN 1083-7450 Journal Code: C2N
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A 3-day monolithic polyacrylate adhesive dispersion type delivery system containing methadone was fabricated and in vitro permeation through hairless mouse and human cadaver skins was conducted. The effect of skin permeation enhancers was also investigated. Skin permeation rate across human cadaver skin was found to be lower than that of hairless mouse. Skin permeation profiles across both types of skins showed a membrane permeation controlled cumulative amount permeated (Q) versus time (t) relationship. Skin permeation rate was found to be dependent on both adhesive film thickness and loading dose of the drug in the matrix. Effective skin permeation rate across the hairless mouse skin was obtained from a patch with 1.5 mm thickness and 15% w/w loading dose. n-Decylmethyl sulfoxide and Azone were found to produce an effective skin permeation rate of methadone through human cadaver skin at a 5% w/w concentration. These initial studies demonstrated the feasibility of methadone administration through intact skin from a transdermal patch.

15/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08804740 96096747 PMID: 8529650
Purification and characterization of a galactose-1-phosphate: UDP-glucose uridyltransferase from the red alga Galdieria sulphuraria.
Gross W; Schnarrenberger C
Freie Universitat Berlin, Institut fur Pflanzenphysiologie und Mikrobiologie, Germany.
European journal of biochemistry (GERMANY) Nov 15 1995, 234 (1) p258-63, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The galactose-1-phosphate uridyltransferase of the red alga Galdieria sulphuraria has been purified about 1800-fold to a final specific activity of approximately 140 U/mg protein. The purification involved chromatography on DEAE-Fractogel, hydroxyapatite, decyl-agarose, and DEAE-Tentacle gel. After SDS/PAGE, the enzyme preparation showed only one protein band of 42 kDa. The enzyme is a homodimer with a molecular mass of 82 kDa as estimated from the sedimentation velocity or 60 kDa as estimated by gel filtration. It has a broad pH optimum between pH 7 and pH 9. The apparent Km values for the forward and backward reactions are Km(Glc1P) = 105 microM, Km(UDP-galactose) = 30 microM, Km(Gal1P) = 400 microM, and Km(UDP-Glc) = 20 microM. The activation energy of the reaction is 45 kJ mol-1. The enzyme is specific for the galactose 1-phosphate to UDP-galactose interconversion in the Leloir pathway while the alternate enzyme for the Isselbacher pathway, UDP-galactose pyrophosphorylase, could not be detected in G. sulphuraria.

15/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08679889 96140882 PMID: 8527599
Blood perfusion and remodelling activity in canine tibial diaphysis after filling with a new bone cement compared to bone wax and poly(methyl methacrylate) cement.
Sturup J; Nimb L; Jensen JS
Department of Orthopaedics U, Rigshopitalet, University of Copenhagen, Denmark.
Biomaterials (ENGLAND) Jul 1995, 16 (11) p845-8, ISSN 0142-9612 Journal Code: A4P
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Six dogs each had one tibia filled with standard poly(methyl methacrylate) (PMMA) bone cement and the contralateral tibia filled with a new methyl methacrylate-n-decyl methacrylate-isobornyl methacrylate (MMA-DMA-IBMA) bone cement (Boneloc) with lowered polymerization heat and monomer leakage. An additional six dogs each had one tibia filled with MMA-DMA-IBMA and the contralateral tibia filled with bone wax. There was a higher diaphyseal blood flow, measured with a microsphere technique, in the legs filled with MMA-DMA-IBMA than in those filled with PMMA. The wax-filled bones presented higher blood perfusion than those with MMA-DMA-IBMA. We found a tendency towards higher 99mtechnetium-labelled methylene diphosphonate (99mTcMDP) uptake, and autoradiograms revealed a tendency towards larger subperiosteal apposition and more blackening, both at the subperiosteal apposition and the cortex, in the bones filled with new bone cement in the first series, but in wax-filled bone in the second series. It is concluded that the new bone cement, compared to standard acrylic bone cement, seems to inhibit the vascular response and bone remodelling activity less, making earlier remodelling possible. However, the new bone cement still seems to inhibit bone blood perfusion compared to bone wax.

15/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08479010 95197652 PMID: 7890754
Identification of the ubiquinone-binding domain in QPs1 of succinate-ubiquinone reductase.
Lee GY; He DY; Yu L; Yu CA
Department of Biochemistry and Molecular Biology, Oklahoma State University, Stillwater 74078.
Journal of biological chemistry (UNITED STATES) Mar 17 1995, 270 (11) p6193-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM30721, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
An azidoubiquinone derivative, 3-azido-2-methyl-5-methoxy [3H]-6-decyl -1,4-benzoquinone ([3H]azido-Q), was used to study the ubiquinone-protein interaction and to identify ubiquinone-binding proteins in bovine heart mitochondrial succinate-ubiquinone reductase. When the reductase was incubated with [3H]azido-Q and illuminated with long wavelength UV light, the decrease in the enzymatic activity correlated with the amount of azido-Q incorporated into the protein. When the illuminated, [3H]azido-Q-treated reductase was extracted with organic solvent and subjected to sodium dodecyl sulfate-polyacrylamide gel electrophoresis, radioactivity was found primarily in the QPs1 subunit. The [3H]azido-Q-labeled QPs1 was purified from labeled reductase by a procedure involving ammonium sulfate fractionation, dialysis, organic solvent extraction, lyophilization, preparative sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and cold acetone precipitation. The purified, [3H]azido-Q-labeled QPs1 protein was subjected to reductive carboxymethylation prior to digestion by trypsin. One azido-Q-linked peptide, with a retention time of 66.9 min, was obtained by high performance liquid chromatographic separation. The partial amino-terminal sequence of this peptide is GLTISQL-, indicating that this tryptic peptide comprises amino acid residues 113-140 of the revised amino acid sequence of QPs1. The Q-binding domain, using the proposed structure of QPs1, is probably located in the stretch connecting transmembrane helices 2 and 3 that extrude from the surface of the M side of the inner membrane.

15/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08415213 94333340 PMID: 8055920
F420H2: quinone oxidoreductase from Archaeoglobus fulgidus. Characterization of a membrane-bound multisubunit complex containing FAD and iron-sulfur clusters.
Kunow J; Linder D; Stetter KO; Thauer RK
Laboratorium fur Mikrobiologie des Fachbereichs Biologie, Philipps-Universitat, Marburg, Germany.
European journal of biochemistry (GERMANY) Jul 15 1994, 223 (2) p503-11, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Archaeoglobus fulgidus, a hyperthermophilic sulfate-reducing archaeon, was found to contain a membrane-bound F420H2: quinone oxidoreductase complex presumed to be involved in energy conservation during growth on lactate plus sulfate. After solubilization with dodecyl-beta-D-maltoside the complex was purified 32-fold with a yield of 24%. Using both gel filtration and native PAGE, an apparent molecular mass of approximately 270 kDa was determined. SDS/PAGE revealed the presence of at least seven polypeptides with apparent molecular masses 56, 45, 41, 39, 37, 33, and 32

kDa. The purified complex contained 1.6 mol FAD, 9 mol non-heme iron and 7 mol acid-labile sulfur/mol complex. It did not contain cytochromes, which were, however, present in the membrane fraction of A. fulgidus (3 nmol/mg membrane protein). The purified F420H2: quinone oxidoreductase complex catalyzed the reduction of 2,3-dimethyl-1,4-naphthoquinone (apparent Km 190 microM) with reduced coenzyme F420 (apparent Km 50 microM) exhibiting a specific activity of 500 U/mg (apparent Vmax) at pH 8.0 (pH optimum) and 65 degrees C (temperature optimum). 2-Methyl-1,4-naphthoquinone (menadione), 2-hydroxy-1,4-naphthoquinone, 1,4-naphthoquinone, 2,3-dimethoxy-5-methyl-1, 4- benzoquinone, and 2,3-dimethoxy-5-methyl-6-decyl-1,4-benzoquinone (decyl -ubiquinone) were also reduced with F420H2, albeit with lower rates. The physiological electron acceptor of the F420H2: quinone oxidoreductase complex is most likely the menaquinone found in the membrane fraction of A. fulgidus.

15/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08137002 94206951 PMID: 8155658
Characterization of the chloroplast cytochrome b6f complex as a structural and functional dimer.
Huang D; Everly RM; Cheng RH; Heymann JB; Schagger H; Sled V; Ohnishi T; Baker TS; Cramer WA
Department of Biological Sciences, Purdue University, West Lafayette, Indiana 47907.
Biochemistry (UNITED STATES) Apr 12 1994, 33 (14) p4401-9, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: GM 38323, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Size analysis of the cytochrome b6f complex by FPLC Superose-12 chromatography and Blue Native PAGE indicated a predominantly dimeric component with M(r) = (1.9-2.5) x 10(5). The true dimer molecular weight including bound lipid, but not detergent, was estimated to be 2.3 x 10(5). Size and shape analysis by negative-stain single-particle electron microscopy indicated that the preparation of dimeric complexes contains a major population that has a protein cross section 40% larger than the monomer, binds more negative stain, and has a geometry with a distinct 2-fold axis of symmetry compared to the monomeric complex. The dimeric species is more stable at higher ionic strength with respect to conversion to the monomeric species. SDS-PAGE of monomer and dimer preparations indicated that both contain the four major polypeptides in approximately equal stoichiometry and also contain the petG M(r) 4000 subunit. One bound chlorophyll a per monomer, part of the bound lipid, is present in monomer and dimer. The in vitro electron-transport activity (decyl -PQH2-->PC-ferricyanide) of the separated dimer was comparable to that of the isolated b6f complex and was 4-5-fold greater than that of the monomer preparation, whose activity could be attributed to residual dimer. No difference in the properties of the dimer and monomer was detected by SDS-PAGE or redox difference spectrophotometry that could account for the difference in activities. However, the concentration of the Rieske [2Fe-2S] center was found by EPR analysis of the gy = 1.90 signal to be lower in the monomer fraction by a factor of 3.5 relative to the dimer.(ABSTRACT TRUNCATED AT 250 WORDS)

15/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07961276 94062335 PMID: 8243059
Purification and immunological characterization of acid beta-galactosidase from dog liver.

Hotamisligil S; Hale S; Alroy J; Fischer I; Raghavan S
Department of Biochemistry, E.K. Shriver Center for Mental Retardation, Waltham, MA 02254.
Comparative biochemistry and physiology (ENGLAND) Oct 1993, 106 (2) p373-82, ISSN 0305-0491 Journal Code: DNV
Contract/Grant No.: HD 05515, HD, NICHD; NINCDS NS 21765, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

1. Dog liver acid beta-galactosidase was isolated in high yield and purified to homogeneity using a series of chromatographies on Con A-Sepharose, decyl -agarose, anion-exchange HPLC and gel-filtration HPLC. 2. Non-denaturing gel filtration by HPLC gave a single homogeneous peak corresponding to molecular mass of 180-190 kDa. During SDS-PAGE analysis, the single peak dissociated into a major band corresponding to molecular mass of 32 kDa with minor bands at 18 and 13 kDa. 3. Polyclonal antibodies raised against the purified enzyme immunoprecipitated beta-galactosidase activity specifically from dog liver extracts and recognized a single 32 kDa band in Western blot analysis of dog tissue homogenates. This antibody did not crossreact with any protein band in tissue homogenates from other species examined except cat. 4. Western blot analysis of tissue extracts from dogs affected with GM1-gangliosidosis showed the presence of a 32 kDa band similar to that of controls.

15/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07924781 93366850 PMID: 8360206
Protein adsorption to poly (ether urethane ureas) modified with acrylate and methacrylate polymer and copolymer additives.
Brunstedt MR; Ziats NP; Robertson SP; Hiltner A; Anderson JM; Lodoen GA; Payet CR
Department of Macromolecular Science, Case Western Reserve University, Cleveland, Ohio 44106.
Journal of biomedical materials research (UNITED STATES) Mar 1993, 27 (3) p367-77, ISSN 0021-9304 Journal Code: HJJ
Contract/Grant No.: HL-25239, HL, NHLBI; HL-33849, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To understand better blood interactions with poly(ether urethane urea) (PEUU) materials, a radioimmunoassay and whole or diluted human plasma were used to characterize the presence of fibrinogen, immunoglobulin G, factor VIII/von Willebrand factor, Hageman factor (factor XII), and albumin on a PEUU formulation and on PEUU formulations modified with the amphiphilic additive Methacrol 2138F (co[diisopropylaminoethyl methacrylate (DIPAM)/decyl methacrylate] [3/1]), or with hydrophobic acrylate or methacrylate polymer or copolymer additives. The protein adsorption assay showed that PEUU films loaded or coated with Methacrol 2138F (Methacrol) or homopoly-DIPAM (h-DIPAM) adsorbed significantly lower amounts of the studied proteins than did either the base PEUU formulations or the PEUUs loaded with the more hydrophobic acrylate or methacrylate polymer additives. Experiments with Methacrol-loaded PEUUs, where the loading of Methacrol was varied from 0.25 wt% to 20.0 wt%, showed that the adsorption of each of the characterized proteins did not vary significantly throughout the Methacrol loading range, and that all Methacrol-loaded PEUU formulations adsorbed significantly lower amounts of the studied proteins than did the unloaded PEUU. Phase separation within the additive loaded PEUUs was characterized by scanning electron microscopy (SEM). The solubility parameters of the additives, as well as of the base PEUU, were calculated and used to interpret differences in phase separation of the additive modified PEUUs. The analysis showed that additives of lower

solubility parameter phase-separated into fewer large microdroplets within the PEUU matrix. SEM analysis also showed that additive microdroplets were not present on the air side surface of loaded PEUUs. To explain the differences in protein adsorption to the air side of additive loaded PEUUs when compared to the base PEUU, it was assumed that the additives near this region of the solvent swollen PEUU matrix may have migrated to, at, or near the PEUU-air interface during film formation, creating an additive enriched PEUU surface region. Once at this surface region, it was suggested that dynamic surface reorientation in response to an aqueous medium ensured that the additives were able significantly to influence protein adsorption behavior only if they interacted with aqueous media more favorably than the PEUU.

15/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07897254 93267588 PMID: 8496914
Long-chain-substituted uric acid and 5,6-diaminouracil derivatives as novel agents against free radical processes: synthesis and in vitro activity.
Fraisse L; Verlhac JB; Roche B; Rascle MC; Rabion A; Seris JL
Groupement de recherche de Lacq, Artix, France.
Journal of medicinal chemistry (UNITED STATES) May 14 1993, 36 (10) p1465-73, ISSN 0022-2623 Journal Code: J0F
Erratum in J Med Chem 1993 Sep 17;36(19) 2832
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A new series of N-alkylated uric acids (2,6,8-purinetrione) and 5,6-diaminouracils (5,6-diamino-2,4-pyrimidinedione) were synthesized, and their activities against free radicals were evaluated. Long-chain derivatives of both series exhibited a large inhibitory activity against oxygen radical induced lipid peroxidation in bovine heart mitochondria (IC50 lower than 1 microM), compared to the reference antioxidants trolox C or alpha-tocopherol. This activity appeared related to (i) the ability of these compounds to reduce the stable radical 1,1-diphenyl-2-picrylhydrazyl and (ii) their lipophilicity estimated by log P determination. In order to study the scavenging mechanisms of diaminouracils and urate derivatives against lipid radicals, they were also tested against the azo-initiated peroxidation of either methyl linoleate in organic solvents or a liposomal suspension of dilinoleoylphosphatidylcholine. Urate derivatives reacted moderately with lipid radicals and were slowly consumed, significantly affecting the propagation of the peroxidation. Diaminouracils strongly reduced the propagation rate. They were quickly consumed and were able to deactivate about 1 mol of lipid radical per mole of compound in organic solvent. Dodecyl urates and decyl- and dodecyldiaminouracils were chosen for further in vitro investigation and in vivo evaluation.

15/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07870170 93216834 PMID: 8463351
Protein adsorption and endothelial cell attachment and proliferation on PAPI-based additive modified poly(ether urethane ureas).
Brunstedt MR; Ziats NP; Schubert M; Stack S; Rose-Caprara V; Hiltner PA; Anderson JM
Department of Macromolecular Science, Case Western Reserve University, Cleveland, OH 44106-4907.
Journal of biomedical materials research (UNITED STATES) Apr 1993, 27 (4) p499-510, ISSN 0021-9304 Journal Code: HJJ
Contract/Grant No.: HL-25239, HL, NHLBI; HL-33849, HL, NHLBI

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To better understand vascular interactions with poly(ether urethane urea) (PEUU) materials, protein adsorption, and endothelial cell attachment and proliferation assays were performed on a base PEUU formulation, on PEUU formulations loaded with hydrophobic and amphiphilic poly (methylene-[polyphenyl isocyanate]) (PAPI) based additives, and on PEUU formulations in which some of the polymer chains had been endcapped with either diisopropylaminoethyl (DIPAA) or decyl (DA) moieties. Protein adsorption experiments with PAPI-based additives showed that additive loaded PEUU formulations adsorbed significantly lower amounts of the studied proteins than did the unloaded PEUU. Protein adsorption to the DA and DIPAA endcapped PEUU films was found not to vary consistently from that of the unloaded PEUU film. Endothelial cell attachment and proliferation experiments with PAPI-DA and polyethylene glycol-PAPI-DA (PEG-PAPI-DA) loaded PEUU films showed that many of the films exhibited attachment and proliferation that was significantly enhanced compared to PEUU A' and that approached or equaled that of the tissue culture polystyrene control. Experiments with PAPI-DIPAA and PEG-PAPI-DIPAA loaded PEUU films exhibited attachment and proliferation data that was often below 10% of the tissue culture polystyrene control values. Experiments with the DA and DIPAA endcapped PEUU films showed endothelial cell attachment and proliferation that was statistically indistinguishable from the PEUU A' values. Contact angle analysis was carried out on the endcapped PEUU films, on the PAPI-based additive loaded PEUU films, and on PEUU A' using the sessile drop method. The advancing and receding contact angle behavior of the PAPI-based additive loaded PEUU films deviated markedly from the behavior of PEUU A', suggesting that the additives were present at the PEUU-water interface. The contact angle behavior of the endcapped PEUUs was similar to that of PEUU A', suggesting that the DA and DIPAA endcap moieties did not exist at the hydrated PEUU surface in appreciable quantities. To explain the differences in protein adsorption and endothelial cell behavior on the air side of additive loaded PEUUs when compared to the base PEUU, it was assumed that the additives near this region of the solvent swollen PEUU matrix may have migrated to, at, or near the PEUU-air interface during film formation, creating an additive enriched PEUU surface region.(ABSTRACT TRUNCATED AT 400 WORDS)

15/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07870168 93216832 PMID: 8463349

Attachment and proliferation of bovine aortic endothelial cells onto additive modified poly(ether urethane ureas).

Brunstedt MR; Ziats NP; Rose-Caprara V; Hiltner PA; Anderson JM; Lodoen GA; Payet CR

Department of Macromolecular Science, Case Western Reserve University, Cleveland, OH 44106-4907.

Journal of biomedical materials research (UNITED STATES) Apr 1993 , 27 (4) p483-92, ISSN 0021-9304 Journal Code: HJJ

Contract/Grant No.: HL-25239, HL, NHLBI; HL-33849, HL, NHLBI

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To better understand endothelial cell interactions with poly(ether urethane urea) (PEUU) materials, and to assess bovine aortic endothelial cell attachment, films were incubated for 24 h with BAEC in media containing 5% fetal bovine serum. Other films were allowed to incubate for 4 more days in media containing 5% fetal bovine serum without cells to assess BAEC proliferation. The assay was performed on PEUU films modified with acrylate and methacrylate polymer and copolymer additives that spanned a wide range on the hydrophobicity/hydrophilicity scale. Tissue culture

polystyrene (TCPS) was used as a control. The assay showed that PEUU films loaded with Methacrol 2138F [copoly(diisopropylaminoethyl methacrylate [DI-PAM]/decyl methacrylate [DM]) (3/1)] or with its hydrophilic component, DIPAM, in homopolymer form (i.e., h-DIPAM), significantly enhanced BAEC attachment (approximately 80% of TCPS values) and proliferation (approximately 80%) when compared to unloaded PEUU films (attachment 73%; proliferation, 47%) or to PEUU films loaded with the more hydrophobic acrylate or methacrylate polymer additives (attachment, 32-69%; proliferation, 18-57%). The assay also showed that PEUU films coated with homopoly(diisopropylaminoethyl acrylate) (h-DIPAA) significantly enhanced BAEC attachment and proliferation when compared to PEUU films coated with h-decyl acrylate (h-DA); films coated with the copolymer of these two acrylates (i.e., co-[DIPAA/DA] [3/1]) showed intermediate behavior. To explain the enhancement of BAEC interaction with films loaded with Methacrol 2138F or h-DIPAM, when compared to unmodified PEUU films or to PEUU films loaded with more hydrophobic acrylate and methacrylate polymer additives, it was assumed that the additives near the surface region of the solvent swollen PEUU matrix may have migrated to, or near to, the PEUU-air interface during film formation, creating an additive enriched PEUU surface region. It is suggested that, once at this surface region, dynamic reorientation in response to an aqueous medium ensured the additives were able significantly to influence protein adsorption, and concomitant endothelial cell behavior, but only if they interacted with aqueous media more favorably than the PEUU. The ability of Methacrol and h-DIPAM additives to enhance endothelial cell behavior is argued to be the result of increased hydrophilicity. This is the result of exposed, hydrogen-bonding DIPAM moieties and increased surface flexibility, which is itself due to the hydration of unhindered Methacrol chains, which may create an additive enriched PEUU-water interfacial zone.

15/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07844079 92165856 PMID: 1537867
Membrane-bound aminopeptidase P from bovine lung. Its purification, properties, and degradation of bradykinin.
Simmons WH; Orawski AT
Department of Molecular and Cellular Biochemistry, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.
Journal of biological chemistry (UNITED STATES) Mar 5 1992, 267 (7) p4897-903, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The membrane-bound form of aminopeptidase P (aminoacylprolyl-peptide hydrolase) (EC 3.4.11.9) was purified to apparent homogeneity from bovine lung microsomes. The enzyme was solubilized using phosphatidylinositol-specific phospholipase C (Bacillus thuringiensis), indicating that bovine lung amino-peptidase P is attached to membranes via a glycosylphosphatidylinositol anchor. The enzyme was purified 1900-fold with a yield of 25% by chromatography on decyl -agarose, omega-aminodecyl-agarose, a second decylagarose column, DEAE-Sephacel, and an ultrafiltration step. Native gradient polyacrylamide gel electrophoresis revealed a single stained protein band whose position in the gel corresponded to cleavage of the Arg1-Pro2 bond of bradykinin. The Mr was 360,000 by gel permeation chromatography and 95,000 by reducing sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The substrate specificity of aminopeptidase P was determined using approximately 50 peptides with proline in the second position. The enzyme could hydrolyze lower NH2-terminal homologs of bradykinin, including Arg-Pro-Pro, which was used as the routine substrate in a rapid fluorescence assay performed in the absence of added Mn2+. Some peptides having NH2-terminal amino acids other than arginine were also cleaved.

Aminopeptidase P appeared to favor peptides that had 2 proline residues or proline analogs in positions 2 and 3 of the substrate. In general, tripeptides having a single proline residue in position 2 were poor substrates. Aminopeptidase P was inhibited by a series of peptides, 3-8 residues long, having an NH2-terminal Pro-Pro sequence. The enzyme was also inhibited by metal-chelating agents, 2-mercaptoethanol (4 mM), p-chloromercuribenzenesulfonic acid, and NaCl at concentrations greater than or equal to 0.25 M. The purified enzyme had a pH optimum of 6.5-7.0 and was most stable in the basic pH range. A role for membrane-bound aminopeptidase P in the pulmonary inactivation of circulating bradykinin is proposed.

15/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07661426 93041867 PMID: 1420264
Sequence analysis of the catalytic subunit of H(+)-ATPase from porcine renal brush-border membranes.
Sander I; Lottspeich F; Appelhans H; Kojro E; Spangenberg J; Weindel C; Haase W; Koepsell H
Max-Planck-Institut fur Biophysik, Frankfurt am Main, Germany.
Biochimica et biophysica acta (NETHERLANDS) Nov 23 1992, 1112 (1) p129-41, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The catalytic subunit of the H(+)-ATPase from brush-border membranes of porcine renal proximal tubules was labeled with the hydrophobic SH-group reagent 10-N-(bromoacetyl)amino-1-decyl -beta-glucopyranoside (BADG) which irreversibly inhibits proton pump activity in the absence but not in the presence of ATP. The labeled protein was purified and digested with proteinases. After isolation and sequencing of proteolytic peptides two BADG-labeled cysteines were identified. The amino acid sequences of the obtained proteolytic peptides were homologous to the catalytic subunit of V-ATPases. From mRNA of porcine kidney cortex a catalytic H(+)-ATPase subunit was cloned. 181 of the 183 amino acids which overlap in the sequence derived from the cDNA and the proteolytic peptides were identical, and the two deviations are due to single base exchanges. A comparison of the amino acid sequence derived from the cloned cDNA with sequences of catalytic H(+)-ATPase subunits communicated by other laboratories revealed 98%, 96% and 94% identity with sequences from bovine adrenal medulla, from bovine kidney medulla and from clathrin-coated vesicles of bovine brain. Between 64% and 69% identity was obtained with sequences from fungi and plants. The data show that the catalytic subunit of V-ATPases is highly conserved during evolution. They indicate organ and species specificity in mammalians.

15/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07456444 92001197 PMID: 1911142
Microheterogeneity of urinary albumin and tubular proteinuria in juvenile diabetes mellitus.
Ries M; Scharer K; Wartha R; Schmidt H; Gekle D
Division of Pediatric Nephrology, University Children's Hospital, Heidelberg, Federal Republic of Germany.
Pediatric nephrology (GERMANY) Sep 1991, 5 (5) p582-6, ISSN 0931-041X Journal Code: AVR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We studied differential urinary albumin excretion by a double

one-dimensional gel electrophoresis with decyl sodium sulphate-polyacrylamide gel electrophoresis in the first, and isoelectric focusing in the second dimension in 37 diabetic children and 20 healthy subjects. In addition, total proteins, albumin, beta 2-microglobulin and molecular size distribution of urinary proteins were measured, the latter using sodium dodecyl sulphate-polyacrylamide gel electrophoresis. Whilst albuminuria was not significantly different from controls we found an increased microheterogeneity of urinary albumin in 38% of patients. In addition, low molecular weight protein (P less than 0.05) and beta 2-microglobulin excretion (P less than 0.01) were elevated. It is suggested that the appearance of highly heterogenous albumin in the pI range of 5.3-5.9 is the result of a decreased tubular reabsorption.

15/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07310807 91115913 PMID: 2277055
Compositional analysis of Biomer.
Belisle J; Maier SK; Tucker JA
3M Company, 3M Center, Corporate Research-Analytical, St. Paul, Minnesota 55144.
Journal of biomedical materials research (UNITED STATES) Dec 1990 , 24 (12) p1585-98, ISSN 0021-9304 Journal Code: HJJ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Biomer, a segmented polyether polyurethane, has been analyzed via hydrolysis/gas chromatography to determine its composition. In addition to the previously reported 4,4'-methylene bis(phenyl isocyanate) (MDI), polytetramethylene glycol (PTMO), and ethylenediamine, we now report the presence of diethylamine, 1,3-diaminocyclohexane and poly (diisopropylaminoethyl methacrylate-co-decyl methacrylate), Biomer's cloudy insoluble phase. In addition, a method is presented to characterize the methacrylate additive by molecular weight based on GPC. Also found by chromatography were the antioxidants Santowhite Powder and BHT. XPS shows no Si (silicone) on the Biomer surface, and a total chloride analysis reports no chloride (less than 0.03%). Time-of-flight SIMS data suggest evidence for the methacrylate additive at the surface, and mass spectroscopy can be interpreted as evidence for a diaminocyclohexane.

15/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07038604 93171245 PMID: 8436583
Protein adsorption onto poly (ether urethane ureas) containing Methacrol 2138F: a surface-active amphiphilic additive.
Brunstedt MR; Ziats NP; Schubert M; Hiltner PA; Anderson JM; Lodoen GA; Payet CR
Department of Macromolecular Science, Case Western Reserve University, Cleveland, Ohio 44106.
Journal of biomedical materials research (UNITED STATES) Feb 1993 , 27 (2) p255-67, ISSN 0021-9304 Journal Code: HJJ
Contract/Grant No.: HL-25239, HL, NHLBI; HL-33849, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Surface characterization and protein adsorption studies were carried out on a series of additive dispersed and additive coated poly(ether urethane ureas), PEUUs, to characterize early events in the blood compatibility of these materials. A hypothesis that is based on surface hydrophilicity, surface flexibility, and adsorption media has been developed to understand the modulated adsorption of plasma proteins by PEUU

additives. Electron spectroscopy for chemical analysis (ESCA) and contact angle analysis were performed on two PEUU formulation as well as on PEUU formulations modified with Methacrol 2138F (co[diisopropylaminoethyl methacrylate (DIPAM)/decyl methacrylate (DM)][3/1]) or acrylate or methacrylate polymer or copolymer analogs of Methacrol 2138F. Methacrol 2138F is a commercially used amphiphilic copolymethacrylate. ESCA showed that the PEUUs loaded with Methacrol 2138F or with its hydrophilic component, homopoly (DIPAM) (h-(DIPAM)), had a higher percentage of nitrogen at their surfaces than did the base PEUUs. Contact angle analysis also showed that the air side of PEUU formulations loaded with Methacrol 2138F were more hydrophobic than was the air side of base PEUUs when films were cast from dimethylacetamide. However, during contact angle testing, the air side of PEUU films loaded with Methacrol 2138F rapidly became more hydrophilic than did the air side of the base PEUU films. A radioimmunoassay and whole or diluted human plasma were also used to characterize the presence of the proteins fibrinogen, immunoglobulin G, factor VIII/von Willebrand factor, Hageman factor (factor XII), and albumin, on the surface of the same PEUUs as analyzed by ESCA and contact angle. The protein adsorption assay showed that PEUU films loaded or coated with Methacrol 2138F, with a copolyacrylate analog of Methacrol 2138F (co(diisopropylaminoethyl acrylate [DIPAA]/decyl acrylate [DA]) [3/1]), or with the hydrophilic polyacrylate or polymethacrylate component analogs of Methacrol 2138F (h-DIPAM or h-DIPAA) adsorbed significantly lower amounts of the proteins than did either the base PEUU formulations or the homopoly(decyl methacrylate) (h-DM) or homopoly(decyl acrylate) (h-DA) coated or loaded PEUUs.

15/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06953568 90202771 PMID: 1690709

The induction of specific rat liver glutathione S-transferase subunits under inadequate selenium nutrition causes an increase in prostaglandin F2 alpha formation.

Chang M; Burgess JR; Scholz RW; Reddy CC

Department of Veterinary Science and Environmental Resources Research Institute, Pennsylvania State University, University Park 16802.

Journal of biological chemistry (UNITED STATES) Apr 5 1990, 265 (10) p5418-23, ISSN 0021-9258 Journal Code: HIV

Contract/Grant No.: CA37979, CA, NCI; HL31245, HL, NHLBI; KO4-HL01240, HL, NHLBI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

We have reported previously that a dietary deficiency in selenium results in an increase in glutathione S-transferase (GST) activity of various rat tissues. In order to verify that the increased GST activity observed in a selenium deficiency results from increased synthesis of GST protein, cytosolic fractions of livers obtained from rats fed selenium-deficient and selenium-supplemented diets were analyzed by Western (protein) blots. Antisera raised against purified individual GST subunits (Ya, Yb, and Yc) were used to detect the corresponding subunits on the blots. The Ya subunit was induced 2.5-fold in the selenium-deficient state. The amount of Yc subunit also increased significantly (p less than 0.05) in selenium deficiency but not to the extent of the Ya subunit. The Yb subunit was not significantly affected by altered selenium nutritional status. A corresponding increase in poly (A) RNAs coding for the Ya and Yc subunits was also observed by Northern blot analysis. Transcriptional activity of GST YaYc genes was elevated by approximately 2-fold in purified nuclei isolated from selenium-deficient rat livers, which is sufficient to account for the increase in YaYc mRNA levels. Therefore, it appears that transcriptional activation of rat liver YaYc genes is the primary cause for the elevation of the corresponding gene products in the selenium-deficient

state. Since the GSTs, especially the isozymes containing Ya subunit, have been implicated in the formation of prostaglandin (PG) F2 alpha, we investigated the effect of selenium deficiency on the PGF2 alpha-forming activity using a specific inhibitor of GSTs, S-decyl-GSH. In rats fed a nutritionally adequate diet, the activity inhibited by S-decyl-GSH accounted for at least half of the conversion of PGH2 to PGF2 alpha. During selenium deficiency, this GST-catalyzed activity was approximately doubled with no change in PGF2 alpha formation by other pathways, resulting in a 2-fold increase in overall synthesis of PGF2 alpha. These data strongly support a role of GSTs, especially those composed of the Ya size subunit, in the synthesis of PGF2 alpha from PGH2.

15/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06871279 92384366 PMID: 1514645
Localization of alveolar surfactant clearance in rabbit lung cells.
Rider ED; Ikegami M; Jobe AH
Department of Pediatrics, Harbor-University of California Los Angeles (UCLA) Medical Center, Torrance 90509.
American journal of physiology (UNITED STATES) Aug 1992, 263 (2 Pt 1) pL201-9, ISSN 0002-9513 Journal Code: 3U8
Contract/Grant No.: HD-11932, HD, NICHD; HD-93301, HD, NICHD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Localization of surfactant phospholipid clearance in lung cells was investigated in vivo in rabbits using radiolabeled dipalmitoylphosphatidylcholine (DPPC) and 1,2-dihexa-decyl -sn-glycero-3-phosphocholine (DPPC-ether), a phospholipase A1- and A2-resistant analogue of DPPC. After intratracheal injection of liposomes of the labeled lipids associated with unlabeled surfactant, adult rabbits were killed in groups of three to five at 0, 4, 12, and 24 h with recovery of bronchoalveolar lavages for alveolar macrophages and surfactant. Type II cells and tissue-associated macrophages were isolated on Percoll gradients following elastase and trypsin digestion of the lungs. Radiolabel recoveries as saturated phosphatidylcholine were measured in alveolar wash, alveolar macrophages, lung tissue, and the type II cell and mixed cell bands from the Percoll gradients. Cost accounting of label demonstrated similar recoveries at 0 h, but significantly more DPPC-ether compared with DPPC in cells at later times, indicating ineffective degradation of the DPPC-ether. Internalization of the lung tissue-associated labels into cells was time dependent. At all times, greater than 65% of the cell-associated labels were recovered in type II cells, indicating the primary role for these cells in clearing alveolar surfactant phospholipid in vivo. The total contribution of alveolar macrophages to the overall clearance was approximately 20%.

15/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06717612 91027803 PMID: 2171651
Anomalies in the electrophoretic resolution of Na+/K(+)-ATPase catalytic subunit isoforms reveal unusual protein--detergent interactions.
Sweadner KJ
Massachusetts General Hospital, Boston 02214.
Biochimica et biophysica acta (NETHERLANDS) Nov 2 1990, 1029 (1) p13-23, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: HL 36271, HL, NHLBI; NS 27653, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Three different isozymes of the Na+/K(+)-ATPase have slightly different different electrophoretic mobilities in sodium dodecyl sulfate (SDS). Certain procedures (reduction and alkylation, heating, and the use of sodium tetradecyl sulfate) have been reported either to improve the electrophoretic separation of isoforms or to reveal the presence of new isoforms. The variables affecting gel electrophoretic mobility were investigated here. Reduction and alkylation decreased the mobility of all three isozymes, and slightly improved the separation of alpha 1 from alpha 2 and alpha 3 without causing a qualitative change in the alpha isoforms detected. Heating the enzyme in SDS caused splitting into two bands. Both bands were intact polypeptides but migrated differently in 5% and 15% polyacrylamide , disclosing an anomalous conformation in detergent. The use of sodium tetradecyl or decyl sulfate instead of dodecyl sulfate altered the relative mobilities of the isozymes, revealing differences in detergent affinity, but no new isoforms were found. In conclusion, Na+/K(+)-ATPase alpha-subunit mobility reflects complex detergent-protein interaction that can be affected by experimental conditions. The existence of more than one band on gels may reflect different conformations in detergent, but should not be accepted alone as evidence for subunit structural heterogeneity.

15/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06650362 90302862 PMID: 2363517
Fibre optic sensor for the detection of potassium using fluorescence energy transfer.
Roe JN; Szoka FC; Verkman AS
Department of Bioengineering, University of California, San Francisco 94143.
Analyst (ENGLAND) Apr 1990, 115 (4) p353-8, ISSN 0003-2654
Journal Code: 4OS
Contract/Grant No.: DK35124, DK, NIDDK; DK39354, DK, NIDDK; HL42368, HL, NHLBI; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A fluorescence fibre optic sensor has been developed for measurement of the potassium concentration in aqueous solution based on the change in optical absorbance of the hydrophobic indicator 7-decyl -2-methyl-4-(3',5'-dichlorophen-4'-one)indonaphth-1-o l (MEDPIN). The sensor was constructed by dipping the distal end of a single optical fibre in a poly(vinyl chloride) (PVC) coating solution containing MEDPIN, a plasticiser, the ionophore valinomycin and the fluorescent dye 1,1'-dioctadecyl-3,3,3',3'-tetramethylindodicarbocyanine perchlorate [DilC1 8(5)]. The change in the absorbance of MEDPIN induced by potassium was detected from the quenching of the fluorescence of DilC18(5) due to energy transfer. Glass slides dipped in the PVC coating solution were used to establish the optical properties of the sensor. The potassium concentration was detected by the absorbance of MEDPIN at 650 nm and by the quenching of the DilC18(5) fluorescence by MEDPIN. The fluorescence intensity and lifetime of DilC18(5) decreased by ca. 40% with the addition of 33 mM KCl, indicating a resonance energy transfer mechanism. Experiments with the fibre optic sensor showed a decrease in the fluorescence of 57% with increasing potassium concentration (0-5 mM) at pH 7.45. The potassium concentration giving a 50% decrease in the fluorescence (Kd) for the most sensitive probe was 0.05 mM KCl. The value of Kd was increased to 1.3 mM when the plasticiser was changed from 2-nitrophenyl octyl ether to tris(2-ethylhexyl)phosphate; however, the 90% response time increased from 10 s to 4.2 min.(ABSTRACT TRUNCATED AT 250 WORDS)

15/3,AB/28 (Item 28 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06603721 88135966 PMID: 3342455
Interaction of surfactants with vesicle membrane of dipalmitoylphosphatidylcholine: fluorescence depolarization study.
Inoue T; Muraoka Y; Fukushima K; Shimozawa R
Department of Chemistry, Faculty of Science, Fukuoka University, Japan.
Chemistry and physics of lipids (NETHERLANDS) Feb 1988, 46 (2) p107-15, ISSN 0009-3084 Journal Code: CZW
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The effect of surfactants on the "fluidity" of dipalmitoylphosphatidylcholine (DPPC) vesicle membrane was studied by means of the fluorescence depolarization technique with fatty acid fluorescent probes, in which the anthroyloxy group is introduced at different positions along the acyl chain. Three types of surfactants were examined; anionic sodium alkylsulfates, cationic alkyltrimethylammonium chlorides, and non-ionic alkanoyl-N-methylglucamides (MEGA-n). Perturbing effects of the surfactants depended on both the alkyl chain-length and the type of head group. Sodium alkylsulfates with octyl- and decyl -chain and alkyltrimethylammonium chlorides with octyl-, decyl - and dodecyl-chain did not affect the membrane fluidity when incorporated in the membrane, whereas sodium dodecylsulfate and tetradecyltrimethylammonium chloride decreased the membrane fluidity at both gel and liquid crystalline states of the membrane. All the MEGA series surfactants decreased the membrane fluidity, whose perturbing potency was in the order of MEGA-8 less than MEGA-9 approximately equal to MEGA-10. The perturbation at different depths in the membrane by sodium dodecylsulfate and MEGA-9 was also examined. No significant change in the fluidity gradient across the membrane was induced by the addition of these surfactants.

15/3,AB/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06601938 88188203 PMID: 3446819
Efficiency, Na+/K+ selectivity and temperature dependence of ion transport through lipid membranes by (221)C10-cryptand, an ionizable mobile carrier.
Castaing M; Lehn JM
Laboratoire de Physiologie Cellulaire, College de France, Paris.
Journal of membrane biology (UNITED STATES) 1987, 97 (2) p79-95, ISSN 0022-2631 Journal Code: J4E
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The kinetics of Na+ and K+ transport across the membrane of large unilamellar vesicles (LUV) were determined at two pH's when transport was induced by (221)C10-cryptand (diaza-1,10-decyl-5-pentaoxa-4,7,13,16,2 1-bicyclo [8.8.5.] tricosane) at various temperatures, and by nonactin at 25 degrees C and (222)C10-cryptand at 20 and 25 degrees C. The rate of Na+ and K+ transport by (221)C10 saturated with the cation and carrier concentrations. Transport was noncooperative and exhibited selectivity for Na+ with respect to K+. The apparent affinity of (221)C10 for Na+ was higher and less pH-dependent than that for K+, and seven times higher than the affinity for Na+ of nonactin. Its enthalpy was higher than that of (222)C10 for K+ ions (20.5 vs. 1.7 kcal . mole-1). The efficiency of (221)C10 transport of Na+ was pH- and carrier concentration-dependent, and was similar to that of nonactin; its activation energy was similar to that for (222)C10 transport of K+ (35.5 and 29.7 kcal . mole-1, respectively). The reaction orders in cation n(S) and in carrier m(M), respectively, increased and decreased as the temperature rose, and were both independent of carrier or cation concentrations; in most cases, they varied slightly

with the pH. n(S) varied with the cation at pH 8.7 and with the carrier for Na+ transport only, while m(M) always depended on the type of cation and carrier. Results are discussed in terms of the structural, physico-chemical and electrical characteristics of carriers and complexes.

15/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06592291 87078690 PMID: 3791565
Pharmacokinetics and tissue distribution of liposome-encapsulated cis-bis-N-decyl-iminodiacetato-1,2-diaminocyclohexane-platinum (II).
Lautersztain J; Perez-Soler R; Khokhar AR; Newman RA; Lopez-Berestein G
Cancer chemotherapy and pharmacology (GERMANY, WEST) 1986, 18 (2) p93-7, ISSN 0344-5704 Journal Code: C9S
Contract/Grant No.: 5511-23, PHS; CA 41581, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The pharmacokinetics and tissue distribution of a lipophilic analogue of cisplatin, cis-bis-N-decyl -iminodiacetato-1,2-diaminocyclohexane platinum (II) (N-decyl -IDP), were studied after the i.v. administration of the free drug in suspension in phosphate-buffered saline (F-N-decyl-IDP) and encapsulated in multilamellar liposomes comprising dimyristoyl phosphatidylcholine and dimyristoyl phosphatidylglycerol at a molar ratio of 7:3 (L-N-decyl-IDP). The encapsulation efficiency and stability at 14 days of L-N-decyl-IDP were greater than 95%. The blood clearance of both forms of the drug fit a two-compartment model. The peak blood level of elemental platinum for L-N-decyl-IDP was fourfold higher than for the free drug (24.2 versus 6.1 micrograms/ml). In consequence, a fourfold difference in the volumes of distribution was observed (176 ml/kg for L-N-decyl-IDP versus 608 ml/kg for F-N-decyl-IDP). Liposome encapsulation reduced the drug clearance by threefold; therefore, the CXT of L-N-decyl-IDP was threefold higher than that of F-N-decyl -IDP (1308 micrograms platinum/ml per min versus 395 micrograms platinum/ml per min). Tissue platinum levels were significantly increased by liposome encapsulation in the lung (33 versus 3.6 micrograms/g), spleen (38.3 micrograms/g versus none detected), and liver (16.2 versus 11.7 micrograms/g), and unchanged in the kidneys. Although only F-N-decyl -IDP resulted in detectable levels of platinum in the small bowel (70.5 micrograms/g), the stool excretion was similar for both forms of the drug. The organ distribution changes secondary to liposome encapsulation may result in an increased antitumor activity of N-decyl-IDP in tumors involving the lung, spleen, and liver, and avoidance of gastrointestinal toxicity.

15/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06314291 87280138 PMID: 3611086
Identification of D-glucose-binding polypeptides which are components of the renal Na+-D-glucose cotransporter.
Neeb M; Kunz U; Koepsell H
Journal of biological chemistry (UNITED STATES) Aug 5 1987, 262 (22) p10718-27, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
D-Glucose-binding polypeptides in the Na+-D-glucose cotransporter from pig renal cortex were identified by affinity labeling with two D-glucose analogs, 10-N-(N-[4-azido-2-nitrophenyl]-beta-alanyl)amino-1-decyl -beta-D- glucopyranoside (NapADG) and 10-N-(bromoacetyl)amino-1-decyl

-beta-D-glucopyranoside (BADG). During short-term incubation in the dark, NapADG and BADG are reversible inhibitors of Na+ gradient-dependent D-glucose uptake and Na+-dependent phlorizin binding with Ki values of about 40 and 400 microM, respectively. Irreversible inhibition of Na+-dependent phlorizin binding, which was prevented by D-glucose or phlorizin, was measured after a 1-h incubation with BADG. Both NapADG and BADG selectively labeled polypeptides with apparent molecular weights of 82,000, 75,000, 64,000, and 47,000. Since labeling of the Mr 82,000 and 75,000 polypeptides by both analogs was partially dependent on the presence of Na+ and was partially protected by D-glucose or phlorizin but not by L-glucose or D-mannose, these polypeptides are thought to be components of the renal Na+-D-glucose cotransporter which contain D-glucose-binding sites. For the Mr 64,000 and 47,000 polypeptides, Na+ dependence and D-glucose protection were not constantly observed. However, also, these polypeptides are thought to be components or proteolytic splitting products of the Na+-D-glucose cotransporter since we observed that three monoclonal antibodies showed cross-reaction with the BADG-labeled Mr 82,000, 64,000, and 47,000 polypeptides (K. Korn, A. Raszeja-Specht, S. Bernotat-Danielowski, and H. Koepsell, manuscript in preparation). When the BADG-labeled Mr 82,000 and 75,000 polypeptides were analyzed after two-dimensional separation by isoelectric focusing and sodium dodecyl sulfate-polyacrylamide gel electrophoresis, three-labeled, D-glucose-protectable polypeptides with the respective molecular weights and isoelectric points of 82,000 and 5.6, 75,000 and 5.4, and 75,000 and 6.9 were distinguished. The data indicate that renal brush-border membranes contain several polypeptides which are components of the Na+-D-glucose cotransporter and contain D-glucose-binding sites.

15/3,AB/32 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06137010 86059370 PMID: 4066668
Human lysosomal acid lipase/cholesteryl ester hydrolase. Purification and properties of the form secreted by fibroblasts in microcarrier culture.
Sando GN; Rosenbaum LM
Journal of biological chemistry (UNITED STATES) Dec 5 1985, 260 (28) p15186-93, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: HL 14230, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Lysosomal acid lipase was purified to near homogeneity in a yield of 25-30% from secretions of human fibroblasts grown on microcarriers in spinner culture. Ammonium chloride was added to the serum-free medium to stimulate production of extracellular enzyme and minimize modifications, including proteolytic processing and destruction of the mannose 6-phosphate recognition marker, that have been associated with packaging and maturation of acid hydrolases in lysosomes. Chromatography of secretions by decyl -agarose, hydroxylapatite, phenylboronate-agarose, and gel filtration resulted in greater than 1500-fold purification of the lipase, representing a 10,000-fold increase above the specific activity of intracellular enzyme. The apparent molecular weight of approximately 49,000, estimated for the lipase by polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate, was similar to that determined for the native enzyme by gel filtration (Mr approximately 47,000). By contrast, a smaller molecular weight (Mr approximately 41,000) was estimated for the intracellular enzyme. The purified enzyme was susceptible to hydrolysis by endo-beta-N-acetylglucosaminidase H, which resulted in at least two new forms, reduced in apparent molecular weight by approximately 4,000-6,000. Treatment with the endoglycosidase did not alter the catalytic activity or heat stability of the acid lipase. However, the treated enzyme was no longer internalized by fibroblasts via the mannose 6-phosphate receptor and thereby had lost the capacity to correct

cholesteryl ester accumulation in cultured lipase-deficient cells. Acid fatty acyl hydrolase activity for cholesteryl oleate, triolein, and methylumbelliferyl oleate co-purified. All three esters were hydrolyzed optimally at pH 4.0, but the pH profile was altered by addition of salts or albumin to the phospholipid-bile salt substrate mixtures. In a series of saturated fatty acyl esters of 4-methylumbelliferone, a derivative with an intermediate chain length (9 carbons) was the best substrate and was hydrolyzed at a rate comparable to that of the oleate ester at pH 4. The optimal pH for hydrolysis of the intermediate and shorter chain length esters was higher by about 2 pH units than that for the longer chain esters (pH approximately 4). The activity of the purified lipase was stimulated by several different proteins. The relationship of this effect to the possible requirement for a natural activator substance has not been determined.(ABSTRACT TRUNCATED AT 400 WORDS)

15/3,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06074597 90028565 PMID: 2804247
Optical measurement of aqueous potassium concentration by a hydrophobic indicator in lipid vesicles.
Roe JN; Szoka FC; Verkman AS
Department of Bioengineering, University of California, San Francisco 94143.
Biophysical chemistry (NETHERLANDS) Jul 1989, 33 (3) p295-302, ISSN 0301-4622 Journal Code: A5T
Contract/Grant No.: DK35124, DK, NIDDK; DK39354, DK, NIDDK; HL42368, HL, NHLBI; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
An assay was developed for K+ in aqueous solution at neutral pH. The method was based on the change in optical absorbance of the hydrophobic indicator 7-(n-decyl)-2-methyl-4-(3',5'-dichlorophen-4'-one)indonapthol++ +-1-ol (MEDPIN) in phospholipid vesicles. Formation of a ternary complex between a valinomycin-K+ pair and the anionic form of MEDPIN in the bilayer resulted in an absorption band at 584 nm. K+ concentration was determined by monitoring the MEDPIN absorbance at 584 nm and MEDPIN quenching of lissamine rhodamine B sulfonylphosphatidylethanolamine (L-RhB-PE) fluorescence by an energy-transfer mechanism. Both the fluorescence intensity and lifetime of L-RhB-PE decreased by more than 25% upon addition of 50 mM K+. Kinetic studies using stopped-flow photometry showed a single-exponential reaction of MEDPIN and valinomycin in vesicles with aqueous K+ (maximum rate 1.7 s-1) that was dependent upon [valinomycin] and [K+]. The lipid surface charge was shown to influence the ratio of anionic to neutral MEDPIN at constant pH, and to alter the sensitivity of MEDPIN absorbance to aqueous [K+]. A 1:20 neutral/negative lipid mole ratio was optimal for K+ detection at pH 7.4. Spectroscopic and kinetic data suggest that the optical response of MEDPIN to K+ involves the formation of a ternary complex between K+, valinomycin and MEDPIN.

15/3,AB/34 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06052519 86200159 PMID: 3701842
Transport of alkali cations through thin lipid membranes by (222)C10-cryptand, an ionizable mobile carrier.
Castaing M; Morel F; Lehn JM
Journal of membrane biology (UNITED STATES) 1986, 89 (3) p251-67, ISSN 0022-2631 Journal Code: J4E
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
The kinetics of K+ and Na+ transport across the membrane of large unilamellar vesicles (L.U.V.) were compared at two pH's, with two carriers: (222)C10-cryptand (diaza-1,10-decyl-5-hexaoxa-4,7,13,16,21,24-bicyclo [8.8.8.]+ ++hexacosane) and valinomcyin, i.e. an ionizable macrobicyclic amino polyether and a neutral macrocyclic antibiotic. The rate of cation transport by (222)C10 saturated as cation and carrier concentrations rose. The apparent affinity of (222)C10 for K+ was higher and less pH dependent than that for Na+ but resembled the affinity of valinomycin for K+. The efficiency of (222)C10 transport of K+ decreased as the pH fell and the carrier concentration rose, and was about ten times lower than that of valinomycin. Noncompetitive K+/Na+ transport selectivity of (222)C10 decreased as pH, and cation and carrier concentrations rose, and was lower than that of valinomycin. Transport of alkali cations by (222)C10 and valinomycin was noncooperative. Reaction orders in cation n(S) and carrier m(M) varied with the type of cation and carrier and were almost independent of pH; n(S) and m(M) were not respectively dependent on carrier or cation concentrations. The apparent estimated constants for cation translocation by (222)C10 were higher in the presence of Na+ than of K+ due to higher carrier saturation by K+, and decreased as pH and carrier concentration increased. Equilibrium potential was independent of the nature of carrier and transported cation. Results are discussed in terms of the structural, physiocochemical and electrical characteristics of carriers and complexes.

15/3,AB/35 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05995019 87004496 PMID: 2944742
Human acid beta-glucosidase: affinity purification of the normal placental and Gaucher disease splenic enzymes on N-alkyl-deoxynojirimycin-sepharose.
Osiecki-Newman KM; Fabbro D; Dinur T; Boas S; Gatt S; Legler G; Desnick RJ; Grabowski GA
Enzyme (SWITZERLAND) 1986, 35 (3) p147-53, ISSN 0013-9432
Journal Code: EI6
Contract/Grant No.: AM 36729, AM, NIADDK; K04-AM 01351, AM, NIADDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Two sepharose-bound 1-deoxynojirimycin N-alkyl derivatives, N-(9-carboxynonyl)- and N-(11-carboxyundecyl)-deoxynojirimycin, were used for the affinity purification of acid beta-glucosidase (beta-Glc) from normal and type-1 Ashkenazi Jewish Gaucher disease (AJGD) sources. The capacities of these nondegradable inhibitor supports were 0.5 and 0.75 mg of normal beta-Glc/ml of settled gel, respectively. The purified normal enzyme (14-18% yield) had a specific activity of 1.6 X 10(6) nmol/h/mg protein and was homogeneous as evidenced by a single protein species of Mr = 67,000 on sodium dodecylsulfate-polyacrylamide gel electrophoresis and reverse phase high-performance liquid chromatography (HPLC). Microsequencing demonstrated a single N terminus, and the sequence of the first 22 N-terminal amino acids was colinear with that predicted from the beta-Glc cDNA. Amino acid composition analyses of beta-Glc revealed a high content (35%) of hydrophobic amino acids. The N-decyl -deoxynojirimycin support facilitated the purification of the residual enzyme from type-1 AJGD spleen to about 7,500-fold in four steps with a yield of about 11%. These new affinity supports provided improved stability, capacity and/or specificity compared to other affinity or HPLC methods for purifying this lysosomal glycosidase.

15/3,AB/36 (Item 36 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05992268 86215064 PMID: 3518703
Preliminary evidence for a processing error in the biosynthesis of Gaucher activator in mucolipidosis disease types II and III.
Ranieri E; Paton B; Poulos A
Biochemical journal (ENGLAND) Feb 1 1986, 233 (3) p763-72, ISSN 0264-6021 Journal Code: 9YO
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Activator protein (AP), which stimulated fibroblast sphingomyelinase activity, was isolated from the spleen of a patient with Gaucher's disease type I by the combined techniques of heat and alcohol denaturation, DEAE-cellulose column chromatography, gel filtration, preparative polyacrylamide-gel electrophoresis and decyl -agarose chromatography. Urea/sodium dodecyl sulphate (SDS)/polyacrylamide-gel electrophoresis showed two bands, one with an Mr of approx. 3,000 and the other with an Mr of 5,000-6,500. Similarly, SDS/polyacrylamide-gel electrophoresis performed in the absence of urea revealed the presence of two components, one of which adsorbed to a concanavalin A (Con A) column. Both components stimulated sphingomyelinase activity. On a non-denaturing polyacrylamide gel containing Triton X-100, four major components, two of which bound to Con A, were detected with the dye Stains-All. Cross-reacting material (CRM) to polyclonal Gaucher spleen AP antibodies was detected in normal fibroblasts and in fibroblasts from patients with sphingomyelinase and beta-glucocerebrosidase deficiency states (Niemann-Pick and Gaucher's diseases respectively). CRM in normal fibroblasts adsorbed to Con A columns and had the same mobility on SDS/ polyacrylamide -gel electrophoresis as Con A-adsorbing Gaucher spleen AP. Normal AP was not observed in mucolipidosis type II (I-cell disease) fibroblasts; instead, extracts from these cells revealed the presence of two closely migrating bands with higher Mr values than normal fibroblast CRM. Furthermore, extracts of media from I-cell fibroblast cultures, but not from control or Gaucher fibroblast cultures, contained AP activity towards sphingomyelinase and beta-glucocerebrosidase. Fibroblasts from a patient with mucolipidosis type III (pseudo-Hurler polydystrophy) showed an intermediate pattern consisting of normal as well as the higher-Mr CRM. Our data provide evidence for the existence of AP in cultured skin fibroblasts and suggest that these proteins may be targetted to the lysosome by post-translational modification in a similar manner to that reported for lysosomal enzymes.

15/3,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05853082 89380669 PMID: 2550496
Comparison of ion-exchange high-performance liquid chromatography columns for purification of Sendai virus integral membrane proteins.
Welling-Wester S; Haring RM; Laurens H; Orvell C; Welling GW
Laboratorium voor Medische Microbiologie, Groningen, The Netherlands.
Journal of chromatography (NETHERLANDS) Aug 4 1989, 476 p477-85, ISSN 0021-9673 Journal Code: HQF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The recovery and separation of the integral membrane proteins, the haemagglutinin-neuraminidase (HN) and the fusion protein (F), from a Sendai virus detergent extract were compared on three different ion-exchange high-performance liquid chromatography (IE-HPLC) columns: Mono Q, TSK DEAE-NPR and Zorbax BioSeries SAX. The detergent, either 1-O-n-octyl-beta-glucopyranoside (octylglucoside) or decyl polyethylene glycol-300 (decyl PEG-300), used for extraction of HN and F proteins from the virions, was also present in the elution buffers at a concentration of 0.1%. Recovery of HN and F proteins was primarily

dependent on the detergent present in the eluent, resulting in yields of HN varying from 18 to 28 and 56 to 67%, when octylglucoside and decyl PEG-300, respectively, were used. The highest yield for HN protein was obtained by separation on either a Mono Q or a TSK DEAE-NPR column with decyl PEG-300 as the additive. Yields of F protein were lower, and the highest recovery of 46% was found in the presence of decyl PEG-300 by separation on the Mono Q column. Analysis of the fractions by sodium dodecyl sulphate-polyacrylamide gel electrophoresis and by size-exclusion HPLC indicated that the HN protein eluted in the presence of decyl PEG-300 from the Mono Q and the TSK DEAE-NPR columns was obtained in pure form, while the F protein was slightly contaminated with HN. Analysis of the fractions with monoclonal antibodies directed against conformational epitopes of HN and F proteins indicated that after IE-HPLC the conformation of the proteins is largely retained.

15/3,AB/38 (Item 38 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05816359 86278559 PMID: 3015999
Size-exclusion high-performance liquid chromatography of Sendai virus membrane proteins in different detergents. A comparison of different columns.
Welling GW; Slopsema K; Welling-Wester S
Journal of chromatography (NETHERLANDS) May 30 1986, 359 p307-14, ISSN 0021-9673 Journal Code: HQF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Four column packings for size-exclusion high-performance liquid chromatography (HPLC) of proteins with particle sizes from 3 to 13 micron were compared, using 0.1% sodium dodecyl sulphate in the solvent. Their suitability for the purification of hydrophobic membrane proteins was studied with Sendai virus proteins as a model. The calibration curves of the two 13-micron column packings were linear up to high molecular weights. In contrast to this, large proteins (greater than 100-150 kD) were eluted later than expected from the 3- and 6-micron packings. Peak capacities for proteins larger than 20 kD ranged from 4.7 to 5.5. Therefore, purification of complex mixtures of membrane proteins will often require rechromatography by a different mode of HPLC. Non-ionic detergents are suitable for further ion-exchange chromatography. The effect of addition of 0.1% of five non-ionic detergents (three gluco-methylalkanamide detergents, octylglucoside, and decyl-polyethyleneglycol-300) to the solvent was investigated and decyl -polyethyleneglycol-300 was found to be most suitable. Size-exclusion HPLC with this detergent resulted in the separation of micelles of three different sizes, of which the larger two contained exclusively the Sendai virus F protein.

15/3,AB/39 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05789491 89088224 PMID: 2850005
Reconstitution of Na+/K+-ATPase into phosphatidylcholine vesicles by dialysis of nonionic alkyl maltoside detergents.
Alpes H; Apell HJ; Knoll G; Plattner H; Riek R
Department of Biology, University of Konstanz, F.R.G.
Biochimica et biophysica acta (NETHERLANDS) Dec 22 1988, 946 (2) p379-88, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The reconstitution of Na+/K+-ATPase from outer medulla of rabbit kidney into large unilamellar liposomes was achieved through detergent

removal by dialysis of mixed micellar solutions of synthetic dioleoyl phosphatidylcholine/octyl glucoside and Na+/K+-ATPase/decyl maltoside or decenyl maltoside. Tight, transport-active liposomes were formed when the lipid and the enzyme were solubilized separately in the nonionic detergents and mixed immediately before starting the dialysis. The two maltoside detergents with different structures of the hydrophobic part of the molecule proved to be well suited for the solubilization of Na+/K+-ATPase with high retention of enzyme activity; the inactivation of enzyme being evidently slower with the unsaturated decenyl maltoside. The diameters of the proteoliposomes, 110 and 170 nm, respectively, were also dependent on the structure of the maltoside detergent, the saturated decyl maltoside producing the bigger liposomes . After freeze-fracture, both preparations exhibited intramembranous particles as structural indicators of successful reconstitution. The electrogenic activity of the reconstituted enzyme was determined by fluorescence measurements with Oxonol VI and by tracer-flux measurements with 22Na+.

15/3,AB/40 (Item 40 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05705385 85283835 PMID: 3161696
Salt soluble cross-linked elastin: formation and composition of fibers.
Manning JN; Davis PF; Greenhill NS; Sigley AJ
Connective tissue research (ENGLAND) 1985, 13 (4) p313-22, ISSN 0300-8207 Journal Code: DQH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cross-linked elastin has been isolated from the salt extract of sheep vascular tissue by means of hydrophobic interaction chromatography on a column of decyl-agarose. Dialysis of the dimethylformamide and sodium dodecyl sulphate column eluates against distilled water produced a precipitate that was fibrous and that resembled insoluble elastin fibers. As judged by amino acid analyses and SDS-polyacrylamide gel electrophoresis, this precipitation resulted in further purification of the soluble cross-linked elastin. Similar chromatography and precipitation of oxalic acid solubilized cross-linked elastin (alpha-elastin) produced identical results.

15/3,AB/41 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05477024 89247556 PMID: 2541801
[Affinity modification of membrane-bound microsomal cytochrome P-450 with lipophilic analogs of substrates]
Affinnaia modifikatsiia membranosviazannogo mikrosomal'nogo tsitokhroma P-450 lipofil'nymi analogami substratov.
Subkhankulova TN; Liakhovich VV; Vainer LM; Reznikov VA
Biokhimiia (USSR) Jan 1989, 54 (1) p17-26, ISSN 0320-9725 Journal Code: A28
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
The following lipophilic spin-labeled cytochrome P-450 analogs were synthesized: 2-octyl-4-(3-iodine-2-oxopropylidene)-2,3,5,5-tetramethylimidaz olidine-1-oxyl (RIII), 2-nonyl-4-(3-iodine-2-oxopropylidene)-2,3,5,5-tetramethylimidaz olidine-1-oxyl (RIV), 2-hepta-decyl-4-(3-iodine-2-oxopropylidene)-2,3,5,5-tetramethyl imidazolidine-1- oxyl (RV). The distribution coefficients, k, in water--lipid and water--octanol systems as well as the theoretical estimates of k for these and previously synthesized analogs, i.e., 4-(3-iodine-2-oxo-propylidenyl)-2,2,3,5,5-pentamethylimidazolid ine-1-oxyl (RI) and 2-hexyl-4-(3-iodine-2-oxopropylidene)-2,3,5,5-tetramethylimi

daz olidine- 1-oxyl (RII) were determined. It was shown that RIII and RIV bind as type I substrates to cytochrome P-450 from rat microsomes induced with phenobarbital or 3-methylcholanthrene as well as to those from control rats. Radicals RIII and RIV inhibit the oxidation of aniline, aminopyrine and benzphetamine. RIII-RV strongly inhibit the O-deethylation of 7-etoxyresorufin. The inhibitory activity of the radicals increases in the following order: RV less than RIV less than or equal to RI less than or equal to RIII less than RII. The experimental results suggest that the inhibitory properties are nonmonotonuesly related to the lipophility. The high lipophility of RIII and its strong inhibitory properties permit to render the latter to the class of inhibitors which can be transported by liposome membrane vehicles to the liver, inhibit the in vivo activity of the microsomal system and thus prolong the effects of drugs oxidized by cytochrome P-450.

15/3,AB/42 (Item 42 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05331669 90036842 PMID: 2808350
Respiration of bloodstream forms of the parasite Trypanosoma brucei brucei is dependent on a plant-like alternative oxidase.
Clarkson AB; Bienen EJ; Pollakis G; Grady RW
Department of Medical and Molecular Parasitology, New York University School of Medicine, New York 10016.
Journal of biological chemistry (UNITED STATES) Oct 25 1989, 264 (30) p17770-6, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: RO1 AI 17899, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
CoQ links the sn-glycerol-3-phosphate dehydrogenase and oxidase components of the cyanide-insensitive, non-cytochrome-mediated respiratory system of bloodstream African trypanosomes. In this and other characteristics, their respiratory system is similar to the alternative oxidase of plants. The parasites contain 206 ng of CoQ9 mg protein-1 which co-sediments with respiratory activity. The redox state of this CoQ responds in a manner consistent with respiratory function: 60% being in the reduced form when substrate is available and the oxidase is blocked; 13% being in the reduced form when the oxidase is functioning and there is no substrate. The addition of CoQ to aceton-extracted cells stimulates salicylhydroxamic acid-sensitive respiration by 56%. After inhibition of respiration by digitonin-mediated dispersal of the electron transport components, liposomes restore 40% of respiratory activity while liposomes containing CoQ restore 66% of this activity. A less hydrophobic analogue, reduced decyl CoQ, serves as a direct substrate for the trypanosome oxidase supporting full salicylhydroxamic acid-sensitive respiration. After digitonin disruption of electron transport, the nonreduced form of this synthetic substrate can reestablish the chain by accepting electrons from dispersed sn-glycerol-3-phosphate dehydrogenase and transferring them to the dispersed oxidase. Similarities between the alternative oxidase of plants and the oxidase of the trypanosome respiratory system include: mitochondrial location, lack of oxidative phosphorylation, linkage of a dehydrogenase and an oxidase by CoQ, lack of sensitivity to a range of mitochondrial inhibitors, and sensitivity to a spectrum of inhibitors which selectively block transfer of electrons from reduced CoQ to the terminal oxidase but do not block electron transfer to the cytochrome bc1 complex of the mammalian cytochrome chain.

15/3,AB/43 (Item 43 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04902505 84000502 PMID: 6615847
The cohydrolases in human spleen that stimulate glucosyl ceramide beta-glucosidase.
Iyer SS; Berent SL; Radin NS
Biochimica et biophysica acta (NETHERLANDS) Oct 17 1983, 748 (1) p1-7, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: NS-03192, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A family of beta-glucosidase-stimulating proteins (called cohydrolase SPH-I here) was isolated from bovine, Gaucher human and control human spleens. All preparations exhibited a similar pattern of four major electrophoretic bands in polyacrylamide when stained with the cationic dye, Stains-All. The bovine bands migrated more rapidly, while the two types of human cohydrolase migrated very similarly. The two human preparations differed in several respects: the concentration was much higher in Gaucher spleen; the Gaucher factors eluted a little earlier from gel permeation and decyl agarose columns; much more of the cohydrolase was bound by a concanavalin A column; the control bands stained less intensely in gels than the Gaucher bands. Antibodies raised in rabbits to bovine cohydrolase reacted with all three preparations. All four bands from Gaucher cohydrolase showed similar ability to stimulate glucosidase and to bind the antibodies. It is evident that the cohydrolases from control and Gaucher spleens are similar in many respects, yet differ in some secondary fashion, possibly in carbohydrate content. It is suggested that Gaucher cohydrolase is formed from normal cohydrolase by the nonenzymatic action of cellular glucose over a period of many years, due to slowed catabolism of the cofactor.

15/3,AB/44 (Item 44 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04804199 82166378 PMID: 6175580
Purification of a Reiter treponemal protein antigen that is immunologically related to an antigen in Treponema pallidum.
Petersen CS; Pedersen NS; Axelsen NH
Infection and immunity (UNITED STATES) Mar 1982, 35 (3) p974-8, ISSN 0019-9567 Journal Code: GO7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A protein antigen called TR-o was isolated from supernatant of a sonically treated Reiter treponeme. The isolation procedure included anion-exchange chromatography on Whatman DE-52, hydrophobic interaction chromatography on decyl agarose, and finally gel filtration on Ac-A-22 Ultrogel. The fractionations were monitored by immunoprecipitation techniques. The recovery was found to be 35%, and the isolated protein was enriched 220 times. The molecular weight of the native protein was estimated to be 550,000 by polyacrylamide gel electrophoresis and 450,000 by gel filtration. Only one 66,000-molecular-weight polypeptide was found by sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the purified protein. The protein was immunologically pure when tested in crossed immunoelectrophoresis against polyspecific rabbit anti-Reiter immunoglobulin, detecting more than 40 treponemal antigens. A monospecific antiserum was raised in rabbits immunized with the purified protein. Monospecific rabbit anti-TR-o gave strong fluorescence with both the Reiter treponeme and Treponema pallidum. The corresponding antigen in T. pallidum could not be demonstrated directly in a crude T. pallidum sonic extract, but rabbit anti-T. pallidum immunoglobulin contained precipitating antibodies against the purified protein. No antibodies against TR-o were found in selected sera from patients with secondary syphilis reactive in traditional syphilis tests.

15/3,AB/45 (Item 45 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04755747 84162142 PMID: 6323468
Purification and characterization of a membrane-associated cAMP-binding protein from developing Dictyostelium discoideum.
Hutchins BL; Frazier WA
Journal of biological chemistry (UNITED STATES) Apr 10 1984, 259 (7) p4379-88, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: NS-13269, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Plasma membranes of 6-h differentiated Dictyostelium discoideum cells contain a cAMP-binding protein with the properties ascribed to the chemotaxis receptor present on these cells. We have purified this cAMP-binding protein using DEAE-Sephadex chromatography, hydrophobic chromatography on decylagarose and preparative polyacrylamide gel electrophoresis in nonionic detergent. Photoaffinity labeling of the DEAE-purified material with 8-azido-[32P] cAMP shows that only an Mr = 70,000 species on sodium dodecyl sulfate gels contains a cAMP-binding site. Two-dimensional polyacrylamide gel electrophoresis of material eluted from decyl -agarose and photoaffinity labeled indicates that the cAMP-binding protein is the most acidic of many Mr = 70,000 proteins present. This method is readily scaled up to process up to 10(11) cells which yield from 25 to 100 micrograms of cAMP-binding protein. Nucleotide specificity studies established that the cAMP-binding site of the protein is similar to that of the cAMP receptor assayed on intact cells and membranes. The rates of association and dissociation of the cAMP-binding protein are extremely rapid as found for the receptor, and its affinity for cAMP is comparable. The cAMP-binding protein is a concanavalin A binding glycoprotein, and is resistant to proteolysis by trypsin, but not chymotrypsin. Like the cAMP receptor in membranes and crude detergent extracts, this cAMP-binding protein is inhibited by phenylmethylsulfonyl fluoride. The purified binding protein exists in solution largely as a monomeric species, with some dimer being detected on gel filtration. Based on these criteria, we conclude that this cAMP binding protein represents the binding subunit of the cAMP chemotaxis receptor.

15/3,AB/46 (Item 46 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04565515 84304972 PMID: 6476366
A study on the separation of reconstituted proteoliposomes and unincorporated membrane proteins by use of hydrophobic affinity gels, with special reference to band 3 from bovine erythrocyte membranes.
Moriyama R; Nakashima H; Makino S; Koga S
Analytical biochemistry (UNITED STATES) Jun 1984, 139 (2) p292-7, ISSN 0003-2697 Journal Code: 4NK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Alkyl-Sepharose 4B with octyl, decyl, or dodecyl groups as an alkyl chain was a good adsorbent for any type of detergents and a variety of proteins, but not for phospholipids in a vesicle form. When these gels were added to the mixtures of reconstituted proteoliposomes prepared by using bovine band 3 and the protein unincorporated into liposomes, free band 3 in solution was adsorbed onto the gels and the proteoliposomes could be recovered by filtration, suggesting that this procedure, when applicable, permits a rapid isolation of proteoliposomes without loss and dilution of the sample. In addition, the results indicated that Bio-Beads

SM-2 resin, which is virtually nonadsorbing for most proteins, can be used in removing any kind of detergents from those protein-detergent mixtures.

15/3,AB/47 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04482271 83266004 PMID: 6874870
Purification of salt-soluble cross-linked elastin by hydrophobic interaction chromatography.
Ryan PA; Manning JN; Davis PF
Journal of chromatography (NETHERLANDS) Jun 10 1983, 275 (1) p31-40, ISSN 0021-9673 Journal Code: HQF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The hydrophobic protein elastin, which is a major constituent of vascular and lung tissue is fragmented in several pathological conditions. The nature of the soluble fragments is not well understood. Such fragments bind to alkyl chains linked to agarose. Elution, which is effected by dimethylformamide and sodium dodecyl sulphate, is optimal from the decyl-agarose column. Dialysis of the eluates against buffered sodium chloride precipitates elastin, thus further purifying the salt-soluble cross-linked elastin.

15/3,AB/48 (Item 48 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04118649 82097008 PMID: 7319546
Biological studies of lipophilic MDP-derivatives incorporated in liposomes.
Jolivet M; Sache E; Audibert F
Immunological communications (UNITED STATES) 1981, 10 (6) p511-22, ISSN 0090-0877 Journal Code: GH4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Adjuvant activities of fatty acid derivatives of N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP) in saline, emulsified in Incomplete Freund Adjuvant (IFA) or incorporated in liposomes were compared. All derivatives were active when given in saline. The potency of MDP-L-Ala-glycerol mycolate was highly enhanced by administration in IFA of after incorporation in liposomes. These procedures had no effect on the activity of MDP-alpha-methyl-gamma-eta-butyl ester and MDP-alpha-methyl-gamma-eta-decyl ester although the presence of MDP could be demonstrated at the surface of the liposomes by anti-MDP antibodies.

15/3,AB/49 (Item 49 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04113224 81111514 PMID: 6780166
Peptide models for protein-mediated cation transport.
Deber CM
Canadian journal of biochemistry (CANADA) Oct 1980, 58 (10) p865-70, ISSN 0008-4018 Journal Code: CHN
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Substances which can perturb the transmembrane cation balance in a predictable manner have wide-ranging uses in the study of cellular processes. We have undertaken to examine transmembrane calcium transport on

the molecular level through the design and synthesis of a series of ionophoric peptides as models for protein-mediated calcium transport. General mechanisms for carrier-mediated membrane transport are discussed. Cation transport profiles are presented for transport by synthetic peptides of structure cyclo(Glu(OR)-Sar-Gly-(N-R1)-Gly)2, where R = benzyl ester or H; R1 = n-decyl or cyclohexyl. Transport of physiologically abundant cations across "liquid membranes" in Pressman cells mediated by cyclo(Glu-Sar-Gly-(N-decyl)Gly)2 was observed to be essentially calcium specific, as long as calcium ions were present in the system. Multilamellar and unilamellar phosphatidylcholine vesicles were each found to be emptied of internal 45Ca2+ ions upon addition of cyclo(Glu(OBz)-Sar-Gly-(N-cyclohexyl)Gly)2 to the vesicle suspension. The results are compared with the naturally occurring calcium ionophore A23187.

15/3,AB/50 (Item 50 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03968828 82142285 PMID: 6277885
Orientation of complex III in the yeast mitochondrial membrane: labeling with [125I] diazobenzenesulfonate and functional studies with the decyl analogue of coenzyme Q as substrate.
Beattie DS; Clejan L; Chen YS; Lin CI; Sidhu A
Journal of bioenergetics and biomembranes (UNITED STATES) Dec 1981, 13 (5-6) p357-73, ISSN 0145-479X Journal Code: HIO
Contract/Grant No.: HD-04007, HD, NICHD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Mitochondria (or mitoplasts) and submitochondrial particles from yeast were treated with [125I] diazobenzenesulfonate to label selectively proteins exposed on the outer or inner surface of the inner mitochondrial membrane. Polyacrylamide gel analysis of the immunoprecipitates formed with antibodies against Complex III or cytochrome b revealed that the two core proteins and cytochrome b were labeled in both mitochondria and submitochondrial particles, suggesting that these proteins span the membrane. Cytochrome c1 and the iron sulfur protein were labeled in mitochondria but not in submitochondrial particles, suggesting that these proteins are exposed on the cytosolic side of the inner membrane. The steady-state reduction of cytochromes b and c1 was determined with succinate and the decyl analogue of coenzyme Q as substrates. Addition of the coenzyme Q analogue to mitochondria caused reduction of 15-30% of ;the total dithionite-reducible b and 100% of the cytochrome c1: Addition of the coenzyme Q analogue to submitochondrial particles led to the reduction of 70% of the total dithionite-reducible cytochrome b but insignificant amounts of cytochrome c1. A model to explain the topography of Complex III in the inner membrane is proposed based on these results.

15/3,AB/51 (Item 51 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03592164 81070115 PMID: 7440713
Radioimmunoassay studies of human apolipoprotein E.
Blum CB; Aron L; Sciacca R
Journal of clinical investigation (UNITED STATES) Dec 1980, 66 (6) p1240-50, ISSN 0021-9738 Journal Code: HS7
Contract/Grant No.: HL 21006, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
This report describes the development and first applications of a sensitive and specific double antibody radioimmunoassay for human apoplipoprotein E (apoE). ApoE was purified from the very low density

lipoproteins of hypertriglyceridemic patients by heparin-agarose affinity chromatography, DEAE-cellulose chromatography, and preparative polyacrylamide gel electrophoresis. The purified apoprotein had an amino acid composition characteristic of apoE and resulted in the production of monospecific antisera when injected into rabbits. The radioimmunoassay, which was carried out in the presence of 5 mM sodium decyl sulfate, had a working range of 0.8-12 ng. The withinassay coefficient of variation was 9% and the coefficient of variation for systematic between-assay variability was 3%. Prior delipidation of samples with organic solvents did not alter their immunoreactivity. In 26 normal volunteers, the mean plasma apoE concentration was 36 +/- 13 microgram/ml. Hyperlipidemic patients (n = 68) had higher mean apoE levels. A single patient with type III hyperlipoproteinemia had a plasma apoE level of 664 microgram/ml. The plasma apoE level was independently related to plasma cholesterol and triglyceride levels in a population of 108 normal and nonchylomicronemic hyperlipidemic patients. The multiple correlation coefficient for this relationship was 0.73. Thus, variation in plasma cholesterol and triglyceride concentrations described 53% of the variation in apoE concentrations in this population. The lipoprotein distribution of apoE was investigated by agarose column chromatography and ultracentrifugation of plasma. Agarose column chromatography demonstrated that all or nearly all plasma apoE is associated with lipoproteins. In plasma from normal volunteers and hypercholesterolemic patients, apoE was found in two discrete lipoprotein classes: very low density lipoproteins and a set of lipoprotein particles with size and density characteristics similar to HDL2. In hypertriglyceridemic patients, nearly all apoE was associated with the triglyceride-rich lipoproteins.

15/3,AB/52 (Item 52 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03419494 79029847 PMID: 81316
Virus-coded origin of a 32,000-dalton protein from avian retrovirus cores: structural relatedness of p32 and the beta polypeptide of the avian retrovirus DNA polymerase.
Schiff RD; Grandgenett DP
Journal of virology (UNITED STATES) Oct 1978, 28 (1) p279-91, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A 32,000-dalton protein (p32) located in avian retrovirus cores was immunoprecipitated from [35S]methionine-labeled avian myeloblastosis virus (AMV) propagated in cultured chicken embryo fibroblast cells by an antiserum preparation (sarc III) derived from tumor-bearing hamsters injected with cloned and passaged cells from an avian sarcoma virus-induced primary hamster tumor. Since sarc III serum apparently contained antibodies only to virus-coded proteins and not to chicken cellular proteins, the immunoprecipitation of p32 from AMV by sarc III serum strongly suggested that p32 is virus coded. The origin of p32 was more definitively established by demonstrating the existence of a structural relationship between p32 and the AMV DNA polymerase. AMV p32 cross-reacted with the beta polypeptide of AMV alphabeta DNA polymerase in radioimmunoprecipitation and radioimmunoprecipitation inhibition assays, indicating that p32 and beta share common antigenic determinants. This relationship was clarified by sodium do-decyl sulfate-polyacrylamide gel electrophoretic analysis of the peptides generated by limited proteolysis of 125I-labeled AMV DNA polymerase polypeptides and of 125I-labeled AMV p32 by chymotrypsin or Staphylococcus aureus V-8 protease. The peptides which appeared during proteolytic digestion of p32 were a subset of those produced by digestion of the beta polypeptide; however, p32 had no discernible peptides in common with the alpha polypeptide. Further, all of the peptides produced by limited proteolysis of beta were present in the digests of either p32 or

alpha. Our findings suggest that p32 is apparently derived by cleavage of the beta polypeptide of AMV DNA polymerase, presumably at a site near or identical to that at which alpha is generated from beta by proteolytic cleavage.

15/3,AB/53 (Item 53 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03397897 80070627 PMID: 229068
Studies on the protein composition of human serum very low density lipoproteins: demonstration of the beta 2-glycoprotein-I.
Polz E; Kostner GM; Holasek A
Hoppe-Seyler's Zeitschrift fur physiologische Chemie (GERMANY, WEST) Aug 1979, 360 (8) p1061-7, ISSN 0018-4888 Journal Code: GB3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human serum VLDL isolated by polyanion precipitation and ultracentrifugation have been delipidated with ethanal/diethyl ether. By electrophoresis in 10% polyacrylamide gels containing 8M urea, we found a protein which comigrated with apolipoprotein E. This protein was purified by column chromatography and turned out to be identical with beta 2-glycoprotein-I, the serum factor which is necessary for the precipitation of triglyceride-rich lipoproteins with sodium decyl sulfate or sodium dodecyl sulfate. Upon analytical isoelectric focusing, beta 2-glycoprotein-I gave four major bands in the pH region 5.7--6.6. All four bands gave an immunochemical reaction of identity with a monospecific antiserum. From its unique amino acid composition we conclude that beta 2-glycoprotein-I is distinct from all apolipoproteins described previously in the literature.

15/3,AB/54 (Item 54 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02921101 77045780 PMID: 990408
Interaction of sodium decyl sulfate with poly(L-ornithine) and poly(L-lysine) in aqueous solution.
Satake I; Yang JT
Biopolymers (UNITED STATES) Nov 1976, 15 (11) p2263-75, ISSN 0006-3525 Journal Code: A5Z
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

15/3,AB/55 (Item 55 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02672123 77022186 PMID: 184835
Radioimmunoassay of apolipoprotein A-I of rat serum.
Fainaru M; Havel RJ; Felker TE
Biochimica et biophysica acta (NETHERLANDS) Sep 28 1976, 446 (1) p56-68, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A double antibody radioimmunoassay technique was developed for quantification of apolipoprotein A-I, the major apoprotein of rat high density lipoprotein. Apo A-I was labeled with 125I by the chloramine-T method. 125I-labeled apo A-I had the same electrophoretic mobility as unlabeled apo A-I and more than 80% of the 125I was precipitated by rabbit anti apo A-I antibodies. The assay is sensitive at the level of 0.5-5 ng,

and has intraassay and interassay coefficients of variation of 4.5 and 6.5% respectively. The specificity of the assay was established by competitive displacement of 125I-labeled apo A-I from its antibody by apo A-I and lipoproteins containing apo A-I, but not by rat albumin and other apoproteins. Immunoreactivity of high density lipoprotein and serum was only about 35% of that of their delipidated forms when Veronal buffer was used as a diluent. Inclusion of 5 mM sodium decyl sulfate in the incubation mixture brought out reactivity equivalent to that found after delipidation. Completeness of the reaction was verified by comparison with the amount of apo A-I in chromatographic fractions of the total apoprotein of high density lipoprotein. Content (weight %, mean values +/- S.D.) of immunoassayable apo A-I was: 62.3 +/- 5.9 in high density lipoprotein; 1.7 +/- 0.3 in low density lipoprotein; 0.09 +/- 0.03 in very low density lipoprotein and 25.0 +/- 5.0 in lymp chylomicrons. Concentration in whole serum was 51.4 +/- 8.9 mg/dl and 33.6 +/- 4.1 mg/dl for female and male rats, respectively (p less than 0.002), equivalent to the sex difference in concentration of high density lipoprotein. 95% of the apo A-I in serum was in high density lipoprotein, 5% in proteins of d greater than 1.21 g/ml and less than 1% in lipoproteins of d less than 1.063 g/ml.

15/3,AB/56 (Item 56 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02327577 76061531 PMID: 1191265
The extraction and characterization of bovine epidermal alpha-keratin.
Steinert PM
Biochemical journal (ENGLAND) Jul 1975, 149 (1) p39-48, ISSN 0264-6021 Journal Code: 9YO
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
1. The alpha-fibrous protein (alpha-keratin) component of bovine epidermis has been extracted and characterized. 2. Prekeratin, a multichain unit of the epidermal tonofilaments, was shown to consist of six different polypeptide chains on polyacrylamide-gel systems containing sodium dodecyl sulphate or sodium decyl sulphate with discontinuous gel buffers, but only three chains were seen when a gel system containing sodium dodecyl sulphate with a continuous gel buffer was used. 3. Extraction of the 'keratinized' stratum corneum and the living part of the epidermis with urea buffers at pH 7.6 or 9.0 released 60% of the total dry weight of the tissues in the form of alpha-helical polypeptides. 4. The numbers, relative amounts and properties of the extracted polypeptides were the same as the subunits of prekeratin and thus are derived from the tonofilaments in situ. 5. The subunits of prekeratin and the polypeptides extracted from the living cell layers contained an average of six cysteine residues, but those from the stratum corneum contained an average of three intrachain disulphide bonds. 6. The polypeptide chains aggregated through non-covalent interactions in vitro into filaments that were similar to the tonofilaments. 7. Since the polypeptides could be released from the stratum corneum without breaking covalent bonds, it is concluded that such bonds do not cross-link the tonofilaments and non-fibrous keratohyalin. It is suggested that the tonofilaments and keratohyalin of bovine epidermis are associated by secondary bonding forces.

15/3,AB/57 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11224273 BIOSIS NO.: 199800005605
Molecular cloning, sequencing, and expression in Escherichia coli of mouse flavin-containing monooxygenase 3 (FMO3): Comparison with the human isoform.

AUTHOR: Falls J Greg; Cherrington Nathan J; Clements Kieran M; Philpot Richard M; Levi Patricia E; Rose Randy L; Hodgson Ernest(a)
AUTHOR ADDRESS: (a)Dep. Toxicol., North Carolina State Univ., Box 7633, Raleigh, NC 27695**USA
JOURNAL: Archives of Biochemistry and Biophysics 347 (1):p9-18 Nov. 1, 1997
ISSN: 0003-9861
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The sequence of mouse flavin-containing monooxygenase 3 (FMO3) was obtained from several clones isolated from a mouse liver cDNA library. The nucleotide sequence of mouse FMO3 was 2020 bases in length containing 37 bases in the 5' flanking region, 1602 in the coding region, and 381 in the 3' flanking region. The derived protein sequence consisted of 534 amino acids including the putative flavin adenine dinucleotide and NADP+ pyrophosphate binding sites (characteristic of mammalian FMOs) starting at positions 9 and 191, respectively. The mouse FMO3 protein sequence was 79 and 82% identical to the human and rabbit FMO3 sequences, respectively. Mouse FMO3 was expressed in Escherichia coli and compared to E. coli expressed human FMO3. The FMO3 proteins migrated with the decyl sulfate-polyacrylamide gel electrophoresis and immunoblotting. The expressed FMO3 enzymes (mouse and human forms) were sensitive to heat and reacted in a similar manner toward metal ions and FMO3 were high toward the substrate methimazole; however, in the presence of trimethylamine and thioacetamide, FMO-dependent methimazole oxidation by both enzymes was reduced by greater than 85%. Other substrates which inhibited methimazole oxidation were thiourea and thiobenzamide and to a lesser degree N,N-dimethylaniline. When probed with mouse FMO3 cDNA, FMO3 transcripts were detected in hepatic mRNA samples from female mice, but not in samples from males. FMO3 was detected in mRNA samples from male and female mouse lung, but FMO3 message was not detected in mouse kidney sample from either gender. Results of immunoblotting confirmed the tissue- and gender-dependent expression of mouse FMO3.

1997

15/3,AB/58 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10052612 BIOSIS NO.: 199598507530
Purification of bovine lens cell-to-cell channels composed of connexin44 and connexin50.
AUTHOR: Konig Nicola; Zampighi Guido A(a)
AUTHOR ADDRESS: (a)Dep. Anatomy Cell Biol., UCLA Sch. Med., Los Angeles, CA **USA
JOURNAL: Journal of Cell Science 108 (9):p3091-3098 1995
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cell-to-cell channels composed of connexin44 and connexin50 were purified from plasma membranes of calf and fetal bovine lenses. The channels were treated with the nonionic detergents octyl-beta-D-glucopyranoside and decyl-beta-D-maltopyranoside, and the channel/detergent complexes purified by ion and gel filtration column chromatography. In negative staining, the channels appeared as annuli 11 +- 0.6 nm (s.d., n = 105) in diameter and as 16 +- 0.8 nm (s.d., n = 96) long particles which corresponded to top and side views of 'complete' cell-to-cell channels. The purified cell-to-cell channels were composed

principally of a protein, called MP70, that appeared as a diffuse 55-75 kDa band in SDS-PAGE. Dephosphorylation with alkaline phosphatase transformed the diffuse 55-75 kDa band into two distinct bands of almost equal intensity. Immunoblotting showed the bands to be connexin44 and connexin50, respectively. The antibodies also recognized weaker bands composed of the unphosphorylated form of both connexins. The connexins appear to be processed independently 'in vivo'. The unphosphorylated form of connexin50 was present in channels and membranes from fetal, calf and adult bovine lenses, while unphosphorylated connexin44 only in channels purified from fetal lenses. Therefore, lens cell-to-cell channels are composed principally of equal amounts of phosphorylated connexins 44 and 50 that appear to be assembled in the same channel ('hybrid').

1995

15/3,AB/59 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09815222 BIOSIS NO.: 199598270140
Effect of axial ligation and delivery system on the tumour-localising and -photosensitising properties of Ge(IV)-octabutoxyphthalocyanines.
AUTHOR: Soncin M; Polo L; Reddi E(a); Jori G; Kenney M E; Cheng G; Rodgers M A J
AUTHOR ADDRESS: (a)Dep. Biol., Univ. Padova, via Trieste 75, I-35121 Padova **Italy
JOURNAL: British Journal of Cancer 71 (4):p727-732 1995
ISSN: 0007-0920
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Four Ge(IV)-octabutoxy-phthalocyanines (GePcs) bearing two alkyl-type axial ligands were assayed for their pharmacokinetic properties and phototherapeutic efficiency in Balb/c mice bearing an intramuscularly transplanted MS-2 fibrosarcoma. The GePcs were i.v. injected at a dose of 0.35 mu-mol kg-1 body weight after incorporation into either Cremophor emulsions or small unilamellar liposomes of dipalmitoyl-phosphatidylcholine (DPPC). Both the nature of the delivery system and the chemical structure of the phthalocyanine were found to affect the behaviour of the GePcs in vivo. Thus, Cremophor-administered GePcs invariably yielded a more prolonged serum retention and a larger association with low-density lipoproteins (LDLs) as compared with the corresponding liposome-delivered phthalocyanines. This led to a greater efficiency and selectivity of turnout targeting. These effects were more pronounced for those GePcs having relatively long alkyl chains (hexyl to decyl) in the axial ligands. Maximal tumour accumulation (0.67 nmol per g of tissue) was found for Ge-Pc(hexyl)-2 at 24 h after injection. Consistently, the Ge-Pc(hexyl)-2, administered via Cremophor, showed the highest phototherapeutic activity towards the MS-2 fibrosarcoma.

1995

15/3,AB/60 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09121703 BIOSIS NO.: 199497130073
The plastoquinone diffusion coefficient in chloroplasts and its mechanistic implications.
AUTHOR: Blackwell Mary(a); Gibas Cynthia; Gygax Scott; Roman Debra; Wagner

Brandee
AUTHOR ADDRESS: (a)Dep. Chemistry, Lawrence Univ., Appleton, WI 54911**USA
JOURNAL: Biochimica et Biophysica Acta 1183 (3):p533-543 1994
ISSN: 0006-3002
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Pyrene fluorescence quenching by plastoquinone (PQ) was used to estimate lateral diffusion coefficients for PQ-9, decyl PQ and PQ-2 in soybean phosphatidylcholine liposomes and in spinach thylakoid and subthylakoid membranes. All three PQs have diffusion coefficients in the range of (0.1-3) cntdot 10-9 cm-2/S in thylakoids and subthylakoids when measured by the pyrene fluorescence quenching technique, values that are at least two orders of magnitude lower than those measured in phosphatidylcholine liposomes. Our values of PQ diffusion coefficients in thylakoids and subthylakoids are at least one order of magnitude below the minimal values estimated by Mitchell et al. (R. Mitchell et al. (1990) Biophys. J. 58, 1011-1024) if the rate of quinol oxidation by the cytochrome bf complex is determined by quinol binding rather than quinol diffusion. Our results, together with those of Mitchell et al., provide evidence that PQ lateral mobility within the thylakoid membrane determines the rate of quinol oxidation by the cytochrome bf complex. We rationalize our results in terms of a percolation model in which PQ mobility is restricted by thylakoid membrane proteins and conclude that plastocyanin rather than PQ must be responsible for rapid electron transport between PS II and PS 1, in agreement with a similar proposal by Lavergne, Joliot and their co-workers (Joliot et al. (1992) Biochim. Biophys. Acta 1101, 1-12; Lavergne et al. (1992) Biochim. Biophys. Acta 1101, 13-22).

1994

15/3,AB/61 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07429347 BIOSIS NO.: 000091035336
RELATIONSHIPS BETWEEN ADSORPTION AND WETTING OF SURFACTANT SOLUTIONS
AUTHOR: GAU C-S; ZOGRAFI G
AUTHOR ADDRESS: SCH. PHARM., UNIV. WIS.-MADISON, MADISON, WIS. 53706.
JOURNAL: J COLLOID INTERFACE SCI 140 (1). 1990. 1-9. 1990
FULL JOURNAL NAME: Journal of Colloid and Interface Science
CODEN: JCISA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Advancing contact angles, .THETA., for aqueous solutions of the nonionic surfactants, penta(oxyethylene) dodecyl monoether, C12E5, and pental (oxyethylene) decyl monoether, C10E5, have been measured on surfaces prepared from polystyrene, PS, and poly(methyl methacrylate), PMMA, latex particles, as well as on paraffin. Whereas with paraffin, wetting of surfactant solutions is the same as with pure liquids at the same surface tension, wetting is increasingly less efficient relative to pure liquids for PS and PMMA. From adhesion tension plots of .gamma.LV cos .THETA. vs .gamma.LV and application of the Gibbs and Young equations it appears, for paraffin, that .GAMMA.SL, the amount adsorbed to the solid-liquid interface, is essentially equal to .GAMMA.LV, the amount adsorbed to the vapor-liquid interface over the entire concentration range, whereas for PS and PMMA, the ratio of .GAMMA.SL to .GAMMA.LV becomes increasingly less than 1, indicative of increasingly less efficient wetting as the solid beocmes more polar. Experimental determinations of .GAMMA.SL and .GAMMA.LV and application of

the Gibbs and Young equations allowed calculation of .GAMMA.LV cos .THETA. and the construction of "estimated" adhesion tension plots. Excellent agreement between plots using contact angle and adsorption data was obtained up to concentrations of surfactant corresponding to surface tensions of about 40 mN/m, thus confirming the important role of .GAMMA.SL relative to .GAMMA.LV to this point in affecting wetting efficiency. At higher surfactant concentrations, but still below the cmc, ratios of .GAMMA.SL to .GAMMA.LV exceed 1, predicting significantly lower contact angles than are actually measured. Such differences are much greater for the more polar solid surface of PMMA than of PS. These latter results are discussed in the context of possible changes in the structure of the adsorbed monolayer at the solid-liquid interface at higher surfactant concentrations.

1990

15/3,AB/62 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06142418 BIOSIS NO.: 000085105570
PAPER SUBSTRATE ROOM-TEMPERATURE PHOSPHORIMETRY OF POLYAROMATIC HYDROCARBONS ENHANCED BY SURFACE-ACTIVE AGENTS
AUTHOR: RAMOS G R; ALVAREZ-COQUE M C G; O'REILLY A M; KHASAWNEH I M; WINEFORDNER J D
AUTHOR ADDRESS: DEP. CHEM., UNIV. FLA., GAINESVILLE, FLA. 32611.
JOURNAL: ANAL CHEM 60 (5). 1988. 416-420. 1988
FULL JOURNAL NAME: Analytical Chemistry
CODEN: ANCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of the presence of surfactants of different character (sodium dodecyl sulfate, sodium decyl sulfate, Brij 35, and dodecyltrimethylammonium chloride) on the paper-substrate room-temperature phosphorescence (PS-RTP) of several polyaromatic hydrocarbons (PAHs) and carbazole was studied. Thallium nitrate was used as heavy-atom perturber. When an anionic surfactant was added or when analytes were spotted from micellar solutions, enhancements of the sensitivity ranging between factors of 2 and 9 were found. On the other hand, the PS-RTP signal was totally quenched in the presence of the cationic surfactant. Similar effects were found for the phosphorescence of the paper background. Absolute limits of detection in the range of 0.2-3 ng were obtained in the presence of sodium dodecyl sulfate. A discussion in the possible mechanisms producing the observed effect is included.

1988

15/3,AB/63 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05615229 BIOSIS NO.: 000083088370
PHARMACOKINETICS AND TISSUE DISTRIBUTION OF LIPOSOME-ENCAPSULATED CIS BIS-N-DECYLIMINODIACETATO-1 2-DIAMINOCYCLOHEXANEPLATINUM-II
AUTHOR: LAUTERSZTAIN J; PEREZ-SOLER R; KHOKHAR A R; NEWMAN R A; LOPEZ-BERESTEIN G
AUTHOR ADDRESS: DEP. OF CLINICAL IMMUNOL. AND BIOLOGICAL THERAPY, UNIV. OF TEXAS, M.D. ANDERS. HOSP. AND TUMOR INST. AT HOUSTON, HOUSTON, TX 77030, USA.
JOURNAL: CANCER CHEMOTHER PHARMACOL 18 (2). 1986 (RECD. 1987). 93-97.

1986
FULL JOURNAL NAME: Cancer Chemotherapy and Pharmacology
CODEN: CCPHD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The pharmacokinetics and tissue distribution of a lipophilic analogue of cisplatin, cis-bis-N-decyl -iminodiacetato-1,2-diaminocyclohexane platinum (II) (N-decyl-IDP), were studied after the i.v. administration of the free drug in suspension in phosphate-buffered saline (F-N-decyl-IDP) and encapsulated in multilamellar liposomes comprising dimyristoyl phosphatidylcholine and dimyristol phosphatidylglycerol at a molar ratio of 7:3 (L-N-decyl-IDP). The encapsulation efficiency and stability at 14 days of L-N-decyl-IDP were greater than 95%. The blood clearance of both forms of the drug fit a two-compartment model. The peak blood level of elemental platinum for L-N-decyl-IDP was fourfold higher than for the free drug (24.2 versus 6.1 .mu.g/ml). In consequence, a fourfold difference in the volumes of distribution was observed (176 ml/kg for L-N-decyl-IDP versus 608 ml/kg for F-N-decyl-IDP). Liposome encapsulation reduced the drug clearance by threefold; therefore, the CXT of L-N-decyl-IDP was threefold higher than that of F-N-decyl-IDP (1308 .mu.g platinum/ml per min versus 395 .mu.g platinum/ml per min). Tissue platinum levels were significantly increased by liposome encapsulation in the lung (33 versus 3.6 .mu.g/g), spleen (38.3 .mu.g/g versus none detected), and liver (16.2 versus 11.7 .mu.g/g), and unchanged in the kidneys. Although only F-N-decyl-IDP resulted in detectable levels of platinum in the small bowel (70.5 .mu.g/g), the stool excretion was similar for both forms of the drug. The organ distribution changes secondary to liposome encapsulation may result in an increased antitumor activity of N-decyl-IDP in tumors involving the lung, spleen, and liver, and avoidance of gastrointestinal toxicity.
1986

15/3,AB/64 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05588409 BIOSIS NO.: 000083061549
FORMATION OF LARGE UNILAMELLAR VESICLES USING ALKYL MALTOSIDE DETERGENTS
AUTHOR: ALPES H; ALLMANN K; PLATTNER H; REICHERT J; RIEK R; SCHULZ S
AUTHOR ADDRESS: FAK. BIOL., UNIV. KONSTANZ, CONSTANCE, FRG.
JOURNAL: BIOCHIM BIOPHYS ACTA 862 (2). 1986. 294-302. 1986
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Several alkyl mltosides having different alkyl chain structures and dodecyl maltotrioside were synthesized. The detergent properties of these compounds were investigated with special emphasis on dialysis kinetics during liposome formation. The critical micelle concentration (CMC) and therefore the speed of detergent removal by dialysis mainly depended on the chain length of the hydrophobic part of the molecule, whereas the number of glucose residues in the polar headgroup had no effect on CMC. Liposome preparation was performed through detergent removal by dialysis combined with adsorption to Amberlite XAD-2 as described by Philippot et al. (Philippot, J.R., Mutafchiev, S. and Liautard, J.P. (1983) Biochem. Biophys. Acta 734, 137-143), leading to a considerable reduction of dialysis volume. Decyl maltoside proved to be a suitable detergent in combination with mixtures of defined synthetic lipids (DOPC/DOPS and DOPC/DOPG). The

presence of at least 10% of negatively charged lipid was essential for the formation of unilamellar liposomes.

1986

15/3,AB/65 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04703399 BIOSIS NO.: 000080006525
SYNTHESIS OF CARBAMYL AND ETHER ANALOGS OF PHOSPHATIDYLCHOLINES
AUTHOR: AGARWAL K; BALI A; GUPTA C M
AUTHOR ADDRESS: DIV. BIOPHYSICS, CENTRAL DRUG RESEARCH INST., LUCKNOW-226001, INDIA.
JOURNAL: CHEM PHYS LIPIDS 36 (2). 1984 (RECD. 1985). 169-178. 1984
FULL JOURNAL NAME: Chemistry and Physics of Lipids
CODEN: CPLIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A complete synthesis of 1-O-hexadecyl-2-O-N-(heptadec-8-cis-enyl)carbamyl-sn-glycero-3-phosphocholine, a novel analog of phosphatidylcholine, was described. Each step is simple to perform and gives the desired products in high yield. Also, some of the intermediates formed during the synthesis were efficiently utilized to prepare 1-O-hexadecyl-2-O-oleoyl-sn-glycero-3-phosphocholine, 1-O-hexadecyl-2-oleoyl-sn-glycero-3-phosphocholine and 3-O-hexadecyl-2-oleoyl-sn-glycero-1-phosphocholine. These phosphatidylcholine (PC) analogs are useful for studying the possible role of phospholipases in the capture and lysis of liposomes in vivo.

1984

15/3,AB/66 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04694526 BIOSIS NO.: 000079107655
APPLICATION OF SYNTHETIC ALKYL GLYCOSIDE VESICLES AS DRUG CARRIERS 1. PREPARATION AND PHYSICAL PROPERTIES
AUTHOR: KIWADA H; NIIMURA H; FUJISAKI Y; YAMADA S; KATO Y
AUTHOR ADDRESS: FACULTY PHARMACEUTICAL SCI., SCI. UNIV. TOKYO, 12 ICHIGAYA FUNAGAWARAMACHI, SHINJUKU-KU, TOKYO 162, JAPAN.
JOURNAL: CHEM PHARM BULL (TOKYO) 33 (2). 1985. 753-759. 1985
FULL JOURNAL NAME: Chemical and Pharmaceutical Bulletin (Tokyo)
CODEN: CPBTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alkyl glycosides formed lamellar vesicles like phosphatidylcholine vesicles (liposomes), and the application of these vesicles as drug carriers was attempted. Various alkyl glycosides were synthesized and vesicles were prepared with these glycosides. The encapsulation capacity of the vesicles was examined in relation to alkyl chain length, sugar moiety and lipid composition. The glucosides of myristyl, cetyl and stearyl alcohols formed vesicles, but those of lauryl, decyl and octyl alcohols did not. The vesicles of glucoside, galactoside and mannoside showed fairly good encapsulation capacity but those of lactoside showed low capacity. An appropriate ratio of glycoside, cholesterol and dicetylphosphate is an important factor for the formation of these vesicles, especially with regard to

dicetylphosphate. The alkyl glycoside vesicles show longer lives on stage in an ampule at 20.degree. C than phosphatidylcholine vesicles. The stability in plasma was also examined. The glycoside vesicles showed rapid release of about 40% of the aqueous contents, but after that, they showed outstanding stability for 48 h in plasma at 37.degree. C. Phosphatidylcholine vesicles showed rapid release of only about 30%, but they disintegrated gradually and showed low encapsulation capacity (about 20%) after 48 h. The application of alkyl glycoside vesicles as drug carriers may be feasible.

1985

15/3,AB/67 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04561914 BIOSIS NO.: 000029084951
EFFECT OF SOME GLYCINE ESTERS ON SULFATE ION TRANSPORT ACROSS MODEL BIOLOGICAL MEMBRANES
AUTHOR: KUCZERA J; JANAS T; PRZESTALSKI S
AUTHOR ADDRESS: DEP. PHYSICS AND BIOPHYS., AGRIC. UNIV. WROCLAW, NORWIDA 25, POL.
JOURNAL: POSTEPY BIOL KOMORKI 11 (3-4). 1984 (RECD. 1985). 527-528. 1984
FULL JOURNAL NAME: Postepy Biologii Komorki
CODEN: PBKOD
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1984

15/3,AB/68 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04325119 BIOSIS NO.: 000078054662
PURIFICATION AND CHARACTERIZATION OF A MEMBRANE ASSOCIATED CYCLIC AMP BINDING PROTEIN FROM DEVELOPING DICTYOSTELIUM-DISCOIDEUM
AUTHOR: HUTCHINS B L M; FRAZIER W A
AUTHOR ADDRESS: DEP. SURG., 300 PASTEUR DR., STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305.
JOURNAL: J BIOL CHEM 259 (7). 1984. 4379-4388. 1984
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Plasma membranes of 6-h differentiated D. discoideum cells contain a cAMP-binding protein with the properties ascribed to the chemotaxis receptor present on these cells. This cAMP-binding protein was purified using DEAE-Sephadex chromatography, hydrophobic chromatography on decylagarose and preparative polyacrylamide gel electrophoresis in nonionic detergent. Photoaffinity labeling of the DEAE-purified material with 8-azido-[32P] cAMP shows that only an MW = 70,000 species on sodium dodecyl sulfate gels contains a cAMP-binding site. Two-dimensional polyacrylamide gel electrophoresis of material eluted from decyl-agarose and photoaffinity labeled indicates that the cAMP-binding protein is the most acidic of many MW = 70,000 proteins present. This method is readily scaled up to process up to 1011 cells which yield from 25 to 100 .mu.g of cAMP-binding protein. Nucleotide specificity studies established that the cAMP-binding site of the protein is similar to that of the cAMP receptor assayed on intact cells and membranes. The rates of association and dissociation of the cAMP-binding

protein are extremely rapid as found for the receptor, and its affinity for cAMP is comparable. The cAMP-binding protein is a concanavalin A binding glycoprotein, and is resistant to proteolysis by trypsin, but not chymotrypsin. Like the cAMP receptor in membranes and crude detergent extracts, this cAMP-binding protein is inhibited by phenylmethylsulfonyl fluoride. The purified binding protein exists in solution largely as a monomeric species, with some dimer being detected on gel filtration. Based on these criteria, it is concluded that this cAMP binding protein represents the binding subunit of the cAMP chemotaxis receptor.

1984

15/3,AB/69 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04321994 BIOSIS NO.: 000078051537
ISOLATION OF A PLATELET MEMBRANE PROTEIN WHICH BINDS THE PLATELET ACTIVATING FACTOR 1-O HEXA DECYL-2-ACETYL-SN GLYCERO 3 PHOSPHORYL CHOLINE
AUTHOR: VALONE F H
AUTHOR ADDRESS: CANCER RES. INST., UNIV. CALIF., SAN FRANCISCO, CALIF. 94143, USA.
JOURNAL: IMMUNOLOGY 52 (1). 1984. 169-174. 1984
FULL JOURNAL NAME: Immunology
CODEN: IMMUA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The phospholipid platelet-activating factor 1-O-hexadecyl-2-acetyl-SN-glycero-3-phosphorylcholine (AGEPC) initiates platelet function by interacting specifically with 1399 .+-. 498 (mean .+-. SD) high-affinity membrane receptors per platelet. In studies designated to characterize the high affinity binding site, AGEPC-human serum albumin-Sepharose was employed to isolate a 180,000 MW protein from human platelet plasma membranes. Platelet plasma membranes were isolated by adsorption of sonicated human platelets to a column of wheat germ agglutinin-Sepharose and elution with N-acetyl-glucosamine. The plasma membranes were solubilized in 5% sodium dodecyl sulfate [SDS] and applied to a column of AGEPC-human serum albumin-Sepharose. After washing the column extensively, the specifically bound material was eluted with a 5-fold molar excess of AGEPC. SDS polyacrylamide gel electrophoresis of the eluted material revealed a single protein with an apparent MW of 180,000. This protein was not recovered from solubilized platelet membranes when chromatography was performed with a column of human serum albumin-Sepharose lacking AGEPC. The capacity of this protein to bind AGEPC suggests that it represents a constituent of the human platelet receptor for AGEPC.

1984

15/3,AB/70 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04270737 BIOSIS NO.: 000078000279
ION SELECTIVE ELECTRODES FOR OCTYL SULFATE AND DECYL SULFATE SURFACTANTS
AUTHOR: KRESHECK G C; CONSTANTINIDIS I
AUTHOR ADDRESS: DEPARTMENT OF CHEMISTRY, NORTHERN ILLINOIS UNIVERSITY, DEKALB, ILLINOIS 60115.
JOURNAL: ANAL CHEM 56 (2). 1984. 152-156. 1984

FULL JOURNAL NAME: Analytical Chemistry
CODEN: ANCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Surfactant ion electrodes were prepared which gave near-Nernstian behavior in aqueous for sodium octyl sulfate at 25.degree. C and sodium decyl sulfate at 20.degree., 25.degree., 30.degree. and 35.degree. C. The selectivity of both electrodes to other alkyl sulfates was determined. The electrode response varied in going from water to pH 7.4 in 0.01 M Tris-HCl buffer with and without 0.1 M NaCl or 6 M urea. The binding of octyl and decyl sulfate to poly(vinylpyrrolidone) (PVP) of different MW, concentration and temperature was also studied. Similar results are given by using equilibrium dialysis or potentiometric titrations with the surfactant electrodes for the binding of decyl sulfate to bovine .beta.-lactoglobulin.

1984

15/3,AB/71 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03922562 BIOSIS NO.: 000076008128
THE INTERACTION OF ARYLAZIDO UBI QUINONE DERIVATIVE WITH MITOCHONDRIAL UBI QUINOL CYTOCHROME C REDUCTASE
AUTHOR: YU L; YU C-A
AUTHOR ADDRESS: DEP. BIOCHEM., OKLA. STATE UNIV., STILLWATER, OKLA. 74078.
JOURNAL: J BIOL CHEM 257 (17). 1982. 10215-10221. 1982
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An arylazido ubiquinone derivative, 2,3-dimethoxy-5-methyl-6-{10-[4-(azido-2-nitroanilinopropionoxy)]-decyl}-1,4-benzoquinone, restores about 60% of the electron transfer activity to [beef heart] ubiquinone- and phospholipid-depleted succinate- or ubiquinol-cytochrome c reductases, compared to that restored by 2,3-dimethoxy-5-methyl-6-(10-bromodecyl)-1,4-benzoquinone. The restored activity is fully sensitive to illumination with long wavelength UV light, suggesting that this azido ubiquinone derivative is bound to the ubiquinone-binding protein at the ubiquinone binding site. Inhibition upon illumination paralleled the amount of azido ubiquinone derivative incorporated into protein. The enzymatic activity of the photolyzed reductase could be restored to a maximum of 40% upon treatment with excess 2,3-dimethoxy-5-methyl-6-(10-bromodecyl)-1,4-benzoquinone. When the the ubiquinone present in the reductase was not removed before addition of the azido ubiquinone derivative, very little inhibition was observed upon illumination under the above conditions, indicating that no exchange between the azido ubiquinone derivative and the intrinsic ubiquinone takes place. If the azido ubiquinone derivative was added to depleted reductase together with 2,3-dimethoxy-5-methyl-6-(10bromodecyl)-1,4-benzoquinone, the maximal activity (that observed when 2,3-dimethoxy-5-methyl-6-(10-bromodecyl)-1,4-benzoquinone alone was used) was obtained. By reacting the 3H-labeled azido ubiquinone derivative with depleted reductase, and performing sodium dodecyl sulfate-polyacrylamide gel electrophoresis after photolysis, the distribution of radioactive ubiquinone derivative among the subunits of ubiquinol-cytochrome c reductase can be obtained. The most heavily labeled subunits were the subunits with mobilities relative to cytochrome c of 0.475 and 0.841 in the Weber and Osborn system. These were

previously identified as cytochrome b proteins. Addition of phospholipids before photolysis had little effect on the distribution pattern of radioactivity. Treatment of the system with antimycin A, which inhibits all the restored activity, also produced no significant effect on the distribution of radioactivity among the subunits, suggesting that antimycin A is not bound to same site as ubiquinone. An Fe S protein inhibitor, 5-n-undecyl-6-hydroxy-4,7-dioxobenzothiazole, also showed little effect on the binding pattern, although it did decrease the total radioactivity incorporated by 25%, suggesting that the inhibitor does not compete directly for the ubiquinone binding site.

1982

15/3,AB/72 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03897237 BIOSIS NO.: 000075075310
PURIFICATION AND POLY PEPTIDE CHARACTERIZATION OF COMPLEX III FROM YEAST MITOCHONDRIA
AUTHOR: SIDHKU A; BEATTIE D S
AUTHOR ADDRESS: DEP. BIOCHEM., MT. SINAI SCH. MED., CITY UNIV. N.Y., NEW YORK, N.Y. 10029.
JOURNAL: J BIOL CHEM 257 (13). 1982. 7879-7886. 1982
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Complex III was isolated and purified from bakers' yeast by ammonium sulfate fractionation and column chromatography on Ultrogel AcA 34. The purified complex contained 7.03 nmol/mg of protein and 4.24 nmol/mg of protein of cytochromes [Cyt] b and c1, respectively. The specific activity of the complex was 17.1 .mu.mol/min/mg of protein, using the decyl analog of coenzyme Q as substrate. Electrophoresis of the purified complex revealed the presence of 7 polypeptides with MW ranging from 15,500 to 50,000. Polypeptides having MW lower than 15,000 were not observed, except when the complex was dissociated in the absence of proteolytic inhibitors, suggesting that these low MW species arise as a result of proteolytic digestion of the complex. The isoelectric points of the subunits of complex III and their stoichiometry were determined. Trypsin and chymotrypsin digestion of the oxidized and reduced forms of the isolated complex suggested that the 2 high MW core proteins are embedded within the complex and are inaccessible to the exogenous proteases, while C b and c1, the Fe-S protein and the 17,500-dalton subunit are substantially exposed to the surface of the complex. The Fe-S protein appears to undergo a conformational change upon reduction of the complex, rendering it less susceptible to trypsin digestion. The core proteins and the Fe-S protein were purified and antibodies against these proteins were raised. Immunoinhibition studies with these antibodies also indicated that the antigenic sites of the core proteins were embedded in the complex.

1982

15/3,AB/73 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03633447 BIOSIS NO.: 000074049024
BIOLOGICAL STUDIES OF LIPOPHILIC N ACETYLMURAMYL-L-ALANYL-D ISO GLUTAMINE DERIVATIVES INCORPORATED IN LIPOSOMES

AUTHOR: JOLIVET M; SACHE E; AUDIBERT F
AUTHOR ADDRESS: GROUPE RECHERCHE NO. 31, C.N.R.S., IMMUNOTHERAPIE EXPERIMENTALE, INSTITUT PASTEUR, 28 DR. ROUX, 75015 PARIS, FRANCE.
JOURNAL: IMMUNOL COMMUN 10 (6). 1981 (RECD. 1982). 511-522. 1981
FULL JOURNAL NAME: Immunological Communications
CODEN: IMLCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Adjuvant activities of fatty acid derivatives of N-acetylmuramyl-L-alanyl-D-isoglutamine (muramyl dipeptide, MDP) in saline, emulsified in incomplete Freund adjuvant (IFA) or incorporated in liposomes were compared. All derivatives were active when given in saline. The potency of MDP-L-Ala-glycerol mycolate was highly enhanced by administration in IFA or after incorporation in liposomes. These procedures had no effect on the activity of MDP-.alpha.-methyl-.gamma.-n-butyl ester and MDP-.alpha.-methyl-.gamma.-n-decyl ester although the presence of MDP could be demonstrated at the surface of the liposomes anti-MDP antibodies. [Adjuvant activity was tested using antibody production in mice and antibody production and elicitation of delayed hypersensitivity in guinea pigs.]

1981

15/3,AB/74 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03578401 BIOSIS NO.: 000073081482
ORIENTATION OF COMPLEX III IN THE YEAST MITOCHONDRIAL MEMBRANE LABELING WITH IODINE-125 LABELED DI AZO BENZENESULFONATE AND FUNCTIONAL STUDIES WITH THE DECYL ANALOG OF COENZYME Q AS SUBSTRATE
AUTHOR: BEATTIE D S; CLEJAN L; CHEN Y-S; LIN C-I P; SIDHU A
AUTHOR ADDRESS: DEP. OF BIOCHEMISTRY, MOUNT SINAI SCH. OF MED. OF THE CITY UNIV. OF N.Y., NEW YORK, N.Y. 10029.
JOURNAL: J BIOENERG BIOMEMBR 13 (5-6). 1981 (RECD. 1982). 357-374. 1981
FULL JOURNAL NAME: Journal of Bioenergetics and Biomembranes
CODEN: JBBID
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Mitochondria (or mitoplasts) and submitochondrial particles from yeast were treated with [125I] diazobenzenesulfonate to label selectively proteins exposed on the outer or inner surface of the inner mitochondrial membrane. Polyacrylamide gel analysis of the immunoprecipitates formed with antibodies against Complex III or cytochrome b revealed that the 2 core proteins and cytochrome b were labeled in both mitochondria and submitochondrial particles, suggesting that these proteins span the membrane. Cytochrome c1 and the iron sulfur protein were labeled in mitochondria but not in submitochondrial particles, suggesting that these proteins are exposed on the cytosolic side of the inner membrane. The steady-state reduction of cytochromes b and c1 was determined with succinate and the decyl analog of coenzyme Q as substrates. Addition of the coenzyme Q analog to mitochondria caused reduction of 15-30% of the total dithionite-reducible b and 100% of the cytochrome c1: Addition of the coenzyme Q analog to submitochondrial particles led to the reduction of 70% of the total dithionite-reducible cytochrome b but insignificant amounts of cytochrome c1. A model to explain the topography of Complex III in the inner membrane is proposed based on these results.

1981

15/3,AB/75 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03511937 BIOSIS NO.: 000073015017
ENTHALPY TITRATION STUDIES OF THE BINDING OF SURFACTANTS TO POLY VINYL PYRROLIDONE
AUTHOR: KRESHECK G C; HARGRAVES W A
AUTHOR ADDRESS: DEP. CHEM., NORTHERN ILLINOIS UNIV., DEKALB, ILL. 60115.
JOURNAL: J COLLOID INTERFACE SCI 83 (1). 1981. 1-10. 1981
FULL JOURNAL NAME: Journal of Colloid and Interface Science
CODEN: JCISA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The temperature dependence of the enthalpy changes that accompany the addition of several surfactants to aqueous polyvinylpyrrolidone solutions was determined by titration calorimetry. The alkyl sulfates (octyl, decyl and dodecyl) showed signs of binding, whereas the dodecylpyridinium halides (bromide and chloride), alkyldimethylphosphine oxides (decyl and dodecyl), and dodecylsarcosinate exhibited only a general solvent effect due to the presence of the polymer (that of a water structure-breaker). The binding of dodecyl sulfate was essentially athermal (although the heat of dilution was more endothermic due to increased dimicellization), and the binding of the octyl and decyl sulfates was endothermic near 25.degree. C. At low dodecyl sulfate binding ratios, the monomeric form of the surfactant reacted with the polymer but 2/3 of the surfactant was bound from the micellar state as saturation was approached. The differences between the binding properties of the various surfactants cannot be explained using existing theories of hydrophobic bonding.

1981

15/3,AB/76 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03341096 BIOSIS NO.: 000072069200
SYNTHESIS OF 2 ACYLAMINO-2-DEOXY-ALPHA-D-GLUCOPYRANOSYL PHOSPHATES MONO SACCHARIDE ANALOGS OF LIPID A
AUTHOR: KISO M; NISHIHORI K; HASEGAWA A
AUTHOR ADDRESS: DEP. AGRICULTURAL CHEMISTRY, GIFU UNIV., KAKAMIGAHARA, GIFU 504, JPN.
JOURNAL: AGRIC BIOL CHEM 45 (2). 1981. 545-548. 1981
FULL JOURNAL NAME: Agricultural and Biological Chemistry
CODEN: ABCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: 3,4,6-Tri-O-acetyl-2-[(tetra-, hexa- and octa-decanoyl and icosanoyl)amino]-2-deoxy-.alpha.-D-glucopyranosyl phosphates (monosaccharide analogs of lipid A; a prominent constituent of endotoxic bacterial lipopolysaccharide) were synthesized from the corresponding 2-(tri-, penta-, hepta- and nona-decyl)-(3,4,6-tri-O-acetyl-1,2-dideoxy-.alpha.-D-glucopyrano)-[2,1-d]-2-oxazol ines.

1981

15/3,AB/77 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03326753 BIOSIS NO.: 000072054857
THE RESPIRATORY CHAIN NADH DEHYDROGENASE OF ESCHERICHIA-COLI ISOLATION OF AN NADH QUINONE OXIDO REDUCTASE FROM MEMBRANES AND COMPARISON WITH THE MEMBRANE BOUND NADH DI CHLORO PHENOL INDOPHENOL OXIDO REDUCTASE
AUTHOR: THOMSON J W; SHAPIRO B M
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. WIS., MADISON, WIS. 53706.
JOURNAL: J BIOL CHEM 256 (6). 1981. 3077-3084. 1981
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An NADH:quinone oxidoreductase that accounts for all of the NADH oxidase activity of E. coli was extracted and purified from membrane preparations. Quinone reduction in intact membranes, or after extraction with Triton X-100, is dependent upon NADH, and NADPH is ineffective. The enzyme was purified 100-fold from membrane extracts by chromatography on AMP-Sepharose, DEAE-Sephacel and Bio-Gel A-1.5M in Triton X-100-containing buffers. This reflects a 2000-fold purification from whole cells, with a 5% yield. The enzyme has an apparent Km for: NADH of 50 .mu.M, decylbenzoquinone of 12 .mu.M, ubiquinone-3 of 40 .mu.M, and dichlorophenolindophenol (DCIP) of 10 .mu.M (the latter substrate exhibits sigmoidal kinetics). The highest Vmax occurs with decylbenzoquinone (75 U/mg) and ubiquinone-3 (50 U/mg); the NADH:quinone oxidoreductase is less active with (DCIP) (Vmax = 7.9 U/mg) and has relatively low activity with ferricyanide, menadione and menaquinone-3. The enzyme responds in a sigmoidal fashion to NADH, with half-maximal activity at 50 .mu.M and substrate inhibition over 200 .mu.M. Triton X-100 acts synergistically with cardiolipin to stimulate the enzyme, with optimal activity found at 0.0125% TX-100, where a 7-fold stimulation by cardiolipin occurs. Deoxycholate inhibits the enzyme both in the presence and absence of lipid. Both the NADH oxidase of intact membranes and the purified NADH:quinone oxidoreductase are inhibited at similar concentrations of 3-n-dodecylmercapto-2-hydroxy-1,4-naphthoquinone. In some preparations up to 95% of the protein of the quinone reductase may be accounted for by a polypeptide of 46,000 daltons, as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. By atomic absorption spectroscopy there is about 1 mol of Fe/46,000 daltons of protein; since the enzyme has no absorption bands in the region 350-700 nm, it may be a non-heme Fe protein. The NADH:quinone oxidoreductase differs from a purified E. coli membrane-bound NADH:DCIP oxidoreductase in its elution from DEAE-cellulose and in its migration on nondenaturing polyacrylamide gels. Four bands of NADH dehydrogenase activity can be found in E. coli membrane extracts separated by gel electrophoresis in buffers containing Triton X-100. One band corresponds to the NADH:DCIP reductase and another to the NADH:quinone reductase. The purified enzymes have different compositions: the NADH:DCIP reductase contains principally a 37,000 dalton polypeptide and the quinone reductase principally a 46,000-dalton polypeptide, with a small amount of 37,000-dalton component. Antiserum prepared against the NADH:DCIP reductase inhibits the crude and purified NADH:quinone reductase activity. The antiserum precipitates the 46,000-dalton polypeptide of the quinone reductase from both purified enzyme preparations and from crude membrane extracts. It also precipitates a 37,000-dalton polypeptide from enzyme preparations and at least 4 polypeptides from crude membrane extracts. The antiserum inhibiting the NADH oxidase is compatible with either or both activities being involved with the respiratory chain-linked enzyme; however, other data suggest that the NADH:quinone reductase is the 1st component of the oxidase pathway.

1981

15/3,AB/78 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03217756 BIOSIS NO.: 000071030867
HYDROPHOBIC ADSORPTION CHROMATOGRAPHY OF PEACH PRUNUS-PERSICA POLY PHENOL OXIDASE
AUTHOR: FLURKEY W H; JEN J J
AUTHOR ADDRESS: DEP. OF AGRICULTURAL CHEMISTRY, WASHINGTON STATE UNIV., PULLMAN, WASH. 99164.
JOURNAL: J FOOD SCI 45 (6). 1980. 1622-1624. 1980
FULL JOURNAL NAME: Journal of Food Science
CODEN: JFDSA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Peach fruit polyphenol oxidase, both crude and pure preparations, adsorb to Phenyl Sepharose, 4-phenylbutylamine Sepharose, CBZ-phenylalanine-TETA-alkyl Sepharose, octyl- and decyl-agarose columns. The enzyme showed no affinity to aminoalkyl agaroses, hydrophobic media with terminal phenol, amino or carboxyl groups on the ligands. The enzyme is weakly hydrophobic and can be purified and characterized with hydrophobic chromatography. Phenyl Sepharose CL-4B columns gave the best separation of isoenzyme forms of the enzyme probably due to biospecific effect in addition to the hydrophobic interactions.

1980

15/3,AB/79 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03104866 BIOSIS NO.: 000020047985
IMMUNO SUPPRESSION IN-VITRO BY AN INHIBITOR OF MEMBRANE PHOSPHO LIPID TURNOVER
AUTHOR: ANDREESEN R; MODOLELL M; SPETH V; MUNDER P G
AUTHOR ADDRESS: MED. UNIVERSITAETSKLIN., FREIBURG, W. GER.
JOURNAL: 12TH MEETING OF THE GESELLSCHAFT FUER IMMUNOLOGIE (SOCIETY FOR IMMUNOLOGY), GARMISCH-PARTENKIRCHEN, GERMANY, OCT. 13-15, 1980.
IMMUNOBIOLOGY 157 (3). 1980. 199. 1980
CODEN: IMMND
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1980

15/3,AB/80 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03030794 BIOSIS NO.: 000070056412
EFFECT OF SOME BENZYL AMMONIUM CHLORIDES ON SULFATE AND CALCIUM ION TRANSPORT ACROSS LIPOSOME MEMBRANES
AUTHOR: GABRIELSKA J; GROBELNY D; KUCZERA J; PRZESTALSKI S; WITEK S; ZYLKA R
AUTHOR ADDRESS: INST. BIOL. BIOPHYS., DEP. PHYS. BIOPHYS., ACAD. AGRIC., NORWIDA 25/27, 50-375 WROCLAW, POL.
JOURNAL: STUD BIOPHYS 77 (3). 1979 (RECD. 1980) 193-200. 1979

FULL JOURNAL NAME: Studia Biophysica
CODEN: STBIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of N-do-decyl -N,N-dimethyl-N-[3-(.beta.-methyl-.beta.-nitrovinyl)-6-methoxybenzyl] ammonium chloride (IA) on Ca2+ and SO42- transport across the membrane of lecithin vesicles is presented. To establish the mechanism of IA activity, the effect of analogs of its fragments, i.e., N-dodecyl-N,N-dimethyl-N-benzylammonium chloride (IB), N-dodecyl-N,N-trimethylammonium chloride (IC) and 4-methoxy-.beta.-methyl-.beta.-nitrostyrene (II) were studied. The rate constants for Ca2+ efflux from, and for SO42- permeation through, the liposome membrane rose rapidly with increasing concentration of IA. The activity of the IB compound was a little lower than that of IA; analog IC acted markedly lower than IA and weaker than IB. For analog II no effect was found in the studied concentration region. The alkyl chain of the studied compounds may enter the lipid bilayer, thus enabling the nitrovinylbenzyl group to interact with the head groups of phospholipid molecules and cause the liposome membrane to loosen. [These findings have relevance to the fungicidal activity of nitrovinyl benzylammonium salts.]

1979

15/3,AB/81 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03029715 BIOSIS NO.: 000070055333
PROTEIN COMPOSITION OF HUMAN SERUM VERY LOW DENSITY LIPO PROTEINS DEMONSTRATION OF BETA-2 GLYCO PROTEIN I
AUTHOR: POLZ E; KOSTNER G M; HOLASEK A
AUTHOR ADDRESS: INST. MED. BIOCHEM., UNIV. GRAZ, HARRACHGASSE 21/III, A-8010 GRAZ, AUSTRIA.
JOURNAL: HOPPE-SEYLER'S Z PHYSIOL CHEM 360 (8). 1979. 1061-1068. 1979
FULL JOURNAL NAME: Hoppe-Seyler'S Zeitschrift fuer Physiologische Chemie
CODEN: HSZPA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Human serum VLDL [very low density lipoprotein] isolated by polyanion precipitation and ultracentrifugation were delipidated with ethanol/diethyl ether. By electrophoresis in 10% polyacrylamide gels containing 8 M urea, a protein was found which co-migrated with apolipoprotein E. This protein was purified by column chromatography and turned out to be identical with .beta.2-glycoprotein-I, the serum factor which is necessary for the precipitation of triglyceride-rich lipoproteins with sodium decyl sulfate or sodium dodecyl sulfate. Upon analytical isoelectric focusing, .beta.2-glycoprotein-I gave 4 major bands in the pH region 5.7-6.6. All 4 bands gave an immunochemical reaction of identity with a monospecific antiserum. From its unique amino acid composition it was concluded that .beta.2-glycoprotein-I is distinct from all apolipoproteins described previously in the literature.

1979

15/3,AB/82 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02956741 BIOSIS NO.: 000069064859
ADJUVANT POLY ARTHRITIS 4. INDUCTION BY A SYNTHETIC ADJUVANT IMMUNOLOGIC HISTO PATHOLOGIC AND OTHER STUDIES
AUTHOR: CHANG Y-H; PEARSON C M; ABE C
AUTHOR ADDRESS: UNIV. CALIF. SCH. MED., REHAB. CENT., 1000 VETERAN AVE., LOS ANGELES, CALIF. 90024, USA.
JOURNAL: ARTHRITIS RHEUM 23 (1). 1980. 62-71. 1980
FULL JOURNAL NAME: Arthritis and Rheumatism
CODEN: ARHEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A solution of an apparently nonimmunogenic synthetic compound, N,N-dioctadecyl-N',N'-bis(2-hydroxyethyl) propanediamine (CP-20961), suspended in mineral oil or olive oil (50 mg/ml), induced acute, chronic polyarthritis when single intradermal injections (0.2 ml) were made in the tail or hindpaw of Lewis rat. The polyarthritis was morphologically almost indistinguishable from classic adjuvant arthritis induced by Freund's complete adjuvant (FCA), a disease generally thought to be the result of a delayed hypersensitivity reaction to a constituent(s) of the injected tubercle bacilli. The disease induced by CP-20961 and that induced by Freund's complete adjuvant followed the same time course and almost identical pattern of development of clinical and histopathologic features. Like the classic adjuvant arthritis, CP-20961 induced arthritis is suppressed by an immunosuppressive agent (cyclophosphamide) or an antiinflammatory drug (phenylbutazone). The alkyldiamine (CP-20961) was potent adjuvant; a dispersion or solution of the compound in mineral oil administered i.p. enhanced the development of the cell-mediated and the humoral immune responses to [mouse leukemia] EL4 cells in the rat. The immunogen responsible for development of adjuvant arthritis is apparently endogenous, e.g., a constituent of host tissue, a viral protein or some complex of the 2.

1980

15/3,AB/83 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02951602 BIOSIS NO.: 000069059720
BENZALKONIUM CHLORIDE SELECTIVE INHIBITOR OF HISTAMINE RELEASE INDUCED BY COMPOUND 48-80 AND OTHER POLY AMINES
AUTHOR: READ G W; KIEFER E F
AUTHOR ADDRESS: PHARMACOL. DEP., UNIV. HAWAII SCH. MED., HONOLULU, HAWAII 96822, USA.
JOURNAL: J PHARMACOL EXP THER 211 (3). 1979 (RECD. 1980). 711-715. 1979
FULL JOURNAL NAME: Journal of Pharmacology and Experimental Therapeutics
CODEN: JPETA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Benzalkonium chloride (BAC) is a mixture of quaternary benzyldimethylalkylammonium chlorides which inhibits histamine release induced by polyamines (48/80 [4-methoxy-N-methylbenzene ethanamine formaldehyde products], ATP, bradykinin, curare, guanethidine, polylysine, polymyxin B, polyTHIQ [polymerized-7-methoxytetrahydroisoquinoline] protamine, stilbamidine or substance P), but not that caused by antigens, concanavalin A, dextran, ionophores (A2318 [2-[(3.beta.,9.alpha.,11.beta.-trimethyl)-8-12-pyrrole carboxymethyl)-1,7-dioxaspiro[6.6]undecyl-2.beta.-methyl]-5-methyl aminobenzoxazol-4-carboxylic acid] or X-537A (lasalocid)), enzymes

(chymotrypsin or phospholipase C), monoamines (dextromethorphan, meperidine or chlorpromazine) or detergents (decylamine, Triton X-100 [polyethylene glycol p-isoctylphenyl ether] or a fire ant venom alkylpiperidine). Inhibition by 1.5 and 3 .mu.g of BAC/ml caused parallel shifts of the 48/80 dose-response curves to the right with no loss of efficacy, indicating that the antagonism was surmountable. Phospholipase C was partially inhibited by BAC, but Triton X-100 inhibited phospholipase C (but not 48/80), indicating that the inhibition of phospholipase C by BAC was probably a nonspecific, detergent effect. BAC caused histamine release by itself at concentrations over 5 .mu.g/ml. Heat inactivation (50.degree. C for 15 min) of the rat mast cells did not prevent this release, suggesting a lytic mechanism for this action. Structure-activity relations studies on various members of the BAC family for their ability to inhibit 48/80-induced histamine release indicated that benzyldimethyltridecylammonium chloride was the most potent.

1979

15/3,AB/84 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02949294 BIOSIS NO.: 000069057412
EFFECT OF THE COMPOSITION OF SODIUM DODECYL SULFATE PREPARATIONS ON THE RENATURATION OF ENZYMES AFTER POLY ACRYLAMIDE GEL ELECTROPHORESIS
AUTHOR: LACKS S A; SPRINGHORN S S; ROSENTHAL A L
AUTHOR ADDRESS: BIOL. DEP., BROOKHAVEN NATL. LAB., UPTON, N.Y. 11973, USA.
JOURNAL: ANAL BIOCHEM 100 (2). 1979 (RECD. 1980). 357-363. 1979
FULL JOURNAL NAME: Analytical Biochemistry
CODEN: ANBCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The extent of renaturation of enzymes after polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate (SDS) depended on the source of the detergent. Analysis of commercial preparations of SDS revealed appreciable amounts of tetradecyl and hexadecyl sulfates in some preparations. Inhibition of renaturation was correlated with the amount of hexadecyl sulfate and to a much lesser extent of tetradecyl sulfate present. The higher alkyl sulfates appeared to bind more tenaciously to proteins in the gel. More extensive washing was required to remove them than to remove dodecyl sulfate, and they were inhibitory to enzyme activity at lower detergent concentrations. A system is described for gas chromatographic analysis of alkyl sulfates containing chains of 10-16 C atoms in length.

1979

15/3,AB/85 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02947172 BIOSIS NO.: 000069055290
ANALYSIS OF PHENYL THIO HYDANTOIN AMINO-ACIDS BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY ON DUPONT ZORBAX CYANO PROPYL SILANE COLUMNS
AUTHOR: JOHNSON N D; HUNKAPILLER M W; HOOD L E
AUTHOR ADDRESS: DIV. BIOL., CALIF. INST. TECH., PASADENA, CALIF. 91125, USA.
JOURNAL: ANAL BIOCHEM 100 (2). 1979 (RECD. 1980). 335-338. 1979
FULL JOURNAL NAME: Analytical Biochemistry
CODEN: ANBCA
RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The phenylthiohydantoins (Pth) of the common amino acids can be resolved in a single analysis using a 25 .times. 0.46 cm DuPont Zorbax cyanopropylsilane (CN) column developed with a gradient of methanol/acetonitrile (17:3) in sodium acetate buffer, pH 5.4. The Zorbax CN columns exhibit greater durability, reproducibility and sensitivity than do columns with an octadecylsilane (C18) support when used for Pth amino acid analysis in automated polypeptide sequencing.

1979

15/3,AB/86 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02907366 BIOSIS NO.: 000069015482
EFFECT OF 8 SURFACTANTS ON TOXICITY OF DIAZINON
AUTHOR: CANDLER W H JR; ROBINSON W H
AUTHOR ADDRESS: DEP. ENTOMOL., VA. POLYTECH. INST. STATE UNIV., BLACKSBURG, VA. 24061, USA.
JOURNAL: MELSHEIMER ENTOMOL SER 0 (25). 1979. 11-15. 1979
FULL JOURNAL NAME: Melsheimer Entomological Series
CODEN: MLESB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Formulations of 8 surfactants were evaluated by topical application to male German cockroaches, Blattella germanica (L.). Diazinon formulated in DMSO, Stoddard's Solvent/acetone and Stoddard's Solvent/acetone plus piperonyl butoxide were also evaluated. All surfactant formulations had a lower LD50 value than diazinon EC. Triton X-100, hexadecyltrimethyl ammonoium bromide, Multi-Film X-77, Tween 80 and Bio-Film formed emulsions that were comparable in toxicity to diazionon in Stoddard's Solvent/acetone. DMSO and piperonyl butoxide formed the most effective preparations with diazinon and had LD50 values significantly lower than all other formulations tested.

1979

15/3,AB/87 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02847310 BIOSIS NO.: 000019017928
FURTHER STUDIES ON THE SELECTIVE INHIBITION OF POLY AMINE INDUCED HISTAMINE RELEASE BY BENZALKONIUM CHLORIDE AND ITS ANALOGS
AUTHOR: READ G W; KIEFER E F
AUTHOR ADDRESS: PHARMACOL. DEP., UNIV. HAWAII, HONOLULU, HAWAII 96822, USA.
JOURNAL: 64TH ANNUAL MEETING OF THE FED. AM. SOC. EXP. BIOL., ANAHEIM, CALIF., USA, APR. 13-18, 1980. FED PROC 39 (3). 1980. ABSTRACT 639. 1980
CODEN: FEPRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1980

15/3,AB/88 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02696239 BIOSIS NO.: 000068006821
THE INTERACTION OF DODECYL AND TETRA DECYL SULFATE WITH PROTEINS DURING POLY ACRYLAMIDE GEL ELECTROPHORESIS
AUTHOR: DOHNAL J C; GARVIN J E
AUTHOR ADDRESS: DIV. CLIN. BIOCHEM., EVANSTON HOSP., EVANSTON, ILL. 60201, USA.
JOURNAL: BIOCHIM BIOPHYS ACTA 576 (2). 1979. 393-403. 1979
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The affinity of tetradecyl sulfate for many unfolded proteins is greater than that of dodecyl sulfate. The presence of tetradecyl sulfate results in the staining of proteins by pinacryptol yellow, seen by Stoklosa and Latz. Some tetradecyl sulfate remains associated with proteins during electrophoresis at room temperature (as opposed to dodecyl sulfate which, within the limit of detection, is completely removed). Tetradecyl sulfate has a greater capacity to dissociate protein aggregates consisting of identical peptide chains, such as glycophorin dimers and bovine serum albumin dimers, than does dodecyl sulfate.

1979

15/3,AB/89 (Item 33 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02677355 BIOSIS NO.: 000067065424
SUSCEPTIBILITY OF LIPO POLY SACCHARIDE DEFECTIVE MUTANTS OF PSEUDOMONAS-AERUGINOSA STRAIN PAO TO DYES DETERGENTS AND ANTIBIOTICS
AUTHOR: KROPINSKI A M B; CHAN L; MILAZZO F H
AUTHOR ADDRESS: DEP. MICROBIOL. IMMUNOL., QUEEN'S UNIV., KINGSTON, ONT., CAN.
JOURNAL: ANTIMICROB AGENTS CHEMOTHER 13 (3). 1978. 494-499. 1978
FULL JOURNAL NAME: Antimicrobial Agents and Chemotherapy
CODEN: AMACC
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Lipopolysaccharide-defective mutants of P. aeruginosa strain PAO were isolated on the basis of their resistance to lipopolysaccharide-specific bacteriophages. These mutants were differentiated by their agglutination in NaCl and acriflavine, phage sensitivity and chemical analysis of the lipopolysaccharides. The susceptibility of the wild-type strain and 4 mutants to a series of 26 agents, including dyes, detergents, antibiotics and lysozyme, was examined. The roughest mutant (AK-43) exhibited increased susceptibility to sodium deoxycholate, hexadecylpyridinium chloride, benzalkonium chloride, ampicillin, penicillin G, erythromycin, colymycin and polymyxin B. The role of cell envelope fractions in antibiotic resistance in P. aeruginosa is discussed.

1978

15/3,AB/90 (Item 34 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02623589 BIOSIS NO.: 000067011649
EFFECTS OF SODIUM OCTYLDECYL SULFATE AND TETRA DECYL SULFATES ON THE

RELEASE OF DIFFERENT PROTEIN FRACTIONS FROM SPINACH THYLAKOID MEMBRANES
AUTHOR: DROBA M; WIECKOWSKI S
AUTHOR ADDRESS: DEP. PLANT BIOCHEM., INST. MOL. BIOL., JAGELLONIAN UNIV., GRODZKA 53, 31-001 KRAKOW, POL.
JOURNAL: BIOCHEM PHYSIOL PFLANZ (BPP) 172 (4). 1978 343-350. 1978
FULL JOURNAL NAME: Biochemie und Physiologie der Pflanzen (Bpp)
CODEN: BPPFA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of low concentrations of sodium octyl, decyl and tetradecyl sulfates on the selective removal of proteins from spinach [Spinacia oleracea] thylakoid membranes was studied. Using differential centrifugation and SDS[sodium dodecyl sulfate]-polyacrylamide gel electrophoresis it was found that all detergents used released 33, 41 and partly 60 kdalton polypeptides more easily than those of 12, 22, 44 and partly 60 kdaltons. Apparently the polypeptides weakly associated with the surface of lamellae or with their hydrophilic regions are removed preferentially when compared with the polypeptides associated with the lipid bilayer of lamellae.

1978

15/3,AB/91 (Item 35 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02448999 BIOSIS NO.: 000066031543
FORMATION OF CLOSED VESICLES FROM A SIMPLE PHOSPHATE DI ESTER PREPARATION AND SOME PROPERTIES OF VESICLES OF DI HEXA DECYL PHOSPHATE
AUTHOR: MORTARA R A; QUINA F H; CHAIMOVICH H
AUTHOR ADDRESS: INST. QUIM., UNIV. SAO PAULO, CP 20780, SAO PAULO, BRAZ.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 81 (4). 1978 1080-1086. 1978
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Upon sonication in water above 55.degree., dihexadecyl phosphate forms aqueous dispersions. Gel filtration, substrate entrapment and EM investigations indicate that these dispersions consist of closed vesicles possessing the characteristics of single bilayer liposomes. These dispersions are quite sensitive to the presence of salts. These wholly synthetic phosphate diester vesicles provide one of the simplest models for the mimicry of membrane and transport functions.

1978

15/3,AB/92 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02441361 BIOSIS NO.: 000066023905
INTERACTION OF SURFACTANT AND HERBICIDE TREATMENTS ON SINGLE CELLS OF LEAVES
AUTHOR: TOWNE C A; BARTELS P G; HILTON J L
AUTHOR ADDRESS: DEP. PLANT SCI., UNIV. ARIZ., TUCSON, ARIZ. 85721, USA.
JOURNAL: WEED SCI 26 (2). 1978 182-188. 1978
FULL JOURNAL NAME: Weed Science
CODEN: WEESA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Enzymatically isolated mesophyll cells of soybean [Glycine max (L.) Merr. 'Kino'] and cotton (Gossypium hirsutum L. 'Stoneville 1613 glandless') were used to study the effects of 3 surfactants, I = 'Sterox SK' (polyoxyethylene thioether), II = 'Renex 36' (polyoxyethylene-6-tridecylether), and III = 'WSCP' [polyoxyethylene (dimethylimino) ethylene (dimethylimino) ethylene dichloride] alone or in combination with 2 herbicides, D-497 (1,1-dimethyl-4,6-diisopropyl-5-indanylethyl ketone) and oryzalin (3,5-dinitro-N4,N4-dipropylsulfanilamide) on cell permeability, photosynthetic 14CO2 fixation and cellular ultrastructure. Greatest amount of efflux of 14C-labeled material from soybean cells was caused by III; other surfactants or herbicides produced only slightly higher effluxes than the controls. Mixtures of oryzalin-I or -II were the only combinations that enhanced efflux in soybean cells above that of cells treated with the surfactant or herbicide alone. However, on cotton cells all surfactants and oryzalin caused considerable leakage but no synergistic effects. Sugars were the predominant compounds leaked from the treated and control cells. Disorganization of all cellular membranes was caused by III; I and II disrupted only the chloroplast grana-intergrana thylakoids, causing abnormal grana. Herbicidal damage to the cell ultrastructure was minimal. Cells treated with combinations of surfactants and herbicides produced only those ultrastructural symptoms that the individual chemicals caused when applied alone. Photosynthetic CO2 fixation was inhibited in both cotton and soybean cells treated with surfactants and (or) herbicides. Interference with membrane integrity, either directly by interaction with membranes or indirectly by interference with cellular energy generating systems that maintain membrane integrity is the postulated mode of action of these surfactants and herbicides.

1978

15/3,AB/93 (Item 37 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02186313 BIOSIS NO.: 000064028828
NMR STUDIES OF THE INTERACTION OF GENERAL ANESTHETICS WITH 1 2 DI HEXA DECYL-SN-GLYCERO-3-PHOSPHORYL CHOLINE BI LAYER
AUTHOR: SHIEH D D; UEDA I; LIN H-C; EYRING H
JOURNAL: PROC NATL ACAD SCI U S A 73 (11). 1976 3999-4002. 1976
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract

ABSTRACT: Sonicated 1,2-dihexadecyl-sn-glycero-3-phosphorylcholine forms liposomes. Studies by Fourier transform PMR of the interaction of these bilayers with some general anesthetics, i.e., chloroform, halothane, methoxyflurane and enflurane, show that the addition of a general anesthetic to the liposomes and raising the temperature have a similar effect in causing the fluidization of the bilayer. General anesthetics act on the hydrophilic site (choline group) in clinical concentrations and then diffuse into the hydrophobic region with the addition of a larger amount of anesthetics. There is evidence that the lecithin choline groups are involved in the interaction with protein and that the general anesthetics change the conformation of some polypeptides and proteins. The general anesthetics, by increasing the motion of positively charged choline groups and negatively charged groups in protein, may weaken the Coulomb-type interaction and cause the lipoprotein conformational changes.

1976

15/3,AB/94 (Item 38 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02174482 BIOSIS NO.: 000064016995
RESOLUTION OF CHLOROPLAST LAMELLAR PROTEINS BY SODIUM TETRA DECYL SULFATE GEL ELECTROPHORESIS
AUTHOR: DROBA M
JOURNAL: BULL ACAD POL SCI SER SCI BIOL 24 (11). 1976 (RECD 1977) 641-645. 1976
FULL JOURNAL NAME: Bulletin de l'Academie Polonaise des Sciences Serie des Sciences Biologiques
CODEN: BAPBA
RECORD TYPE: Abstract

ABSTRACT: The effect of sodium tetradecyl sulfate (STS) on solubility and electrophoretic resolution of spinach [Spinacia oleracea] thylakoid membrane proteins was studied. STS-polyacrylamide gel electrophoresis yielded 10 polypeptide fractions whose MW ranged from 21-150 kilodaltons. The polypeptides of 21-60 kilodalton range are similar to those released by SDS treatment. These are probably cytochromes f and b6, CF1 [chloroplast coupling factor 1] and some polypeptides which are components of the pigment-protein complexes of PS I and PS II[photosystems].
1976

15/3,AB/95 (Item 39 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02164210 BIOSIS NO.: 000064006719
ATP AND OTHER NUCLEOTIDE INTERACTION WITH MODEL COMPOUNDS OF AMINO-ACIDS
AUTHOR: HIDESHIMA T; KIMIZUKA H; ABOOD L G; TANAKA R
JOURNAL: J THEOR BIOL 65 (1). 1977 15-27. 1977
FULL JOURNAL NAME: Journal of Theoretical Biology
CODEN: JTBIA
RECORD TYPE: Abstract

ABSTRACT: With the use of a new liquid scintillation technique, the partitioning and interfacial interaction of 3H-ATP and other adenine nucleotides to various amphiphiles was studied. The amphiphiles consisted of lipophilic groups attached to amino acid residues or certain functional groups and were as follows: trimethylindole, octadecylamine, octadecylalcohol, dodecylguanidine, stearylamide, acetododecylamide, p-nonylphenol, stearylmercaputan, stearic acid and imidazole. A toluene solution containing the lipophilic substance and fluor molecules was layered onto aqueous solutions containing a 3H-nucleotide, and the interaction followed by the liquid scintillation technique. A strong interaction with the nucleotides occurred with dodecylguanidine, octadecylamine and trimethylindole, while the interaction with the other amphiphiles was slight or absent. The time course of the interaction followed 1st order kinetics irrespective of the number of reactive species; the rate of diffusion of the nucleotide being the rate-determining step. The technique permitted a simple analysis of formation constants; which for ATP were 1-2 orders of magnitude greater than for ADP and AMP. In the presence of Ca2+, but not Mg2+, an interaction occurred between ATP and either stearic acid, stearyl mercaputan and p-nonyl phenol. In the presence of Mg2+, but not Ca2+, an interaction occurred between stearic acid and polyadenylic acid. The results are discussed in relation to ATP interactions with proteins

and lipids.

1977

15/3,AB/96 (Item 40 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02091435 BIOSIS NO.: 000063006422
MOLECULAR AGGREGATION OF THE SLOW REACTING HEMOLYTIC LYSO LECITHIN ANALOG 1 OCTA DECYL-2-BENZYL GLYCERO 3 PHOSPHORYL CHOLINE IN AQUEOUS SOLUTION
AUTHOR: WELTZIEN H U; ARNOLD B; BLUME A; KALKOFF H G
JOURNAL: CHEM PHYS LIPIDS 16 (4). 1976 267-275. 1976
FULL JOURNAL NAME: Chemistry and Physics of Lipids
CODEN: CPLIA
RECORD TYPE: Abstract

ABSTRACT: An attempt was made to relate the retarded adsorption to [human] red cells of the slow reacting hemolytic phosphatide dl-1-octadecyl-2-benzyl-glycero-3-phosphorylcholine (benzyl-lysolecithin) to its aggregation status in aqueous solution. Light scattering measurements indicated a critical micelle concentration at 37.degree. of less than 2 .times. 10-6 M. The micellar weight as determined by angle dependent light scattering was 6 .times. 107 with about 97,000 molecules/micelle. The aggregates, which according to EM observations were more similar to lecithin-liposomes than to usual lysolecithin-micelles, underwent a phase transition at 14.degree. from a tightly packed liquid-crystalline state to the looser structure of a gel phase with increased mobility of the aliphatic chains. The enthalpy of transition was 4.2 kcal/mol. These changes of the micellar structure were reflected in the binding kinetics of benzyl-lysolecithin to red cells in that the binding rate was rather constant below, but strongly increasing above the transition temperature. The unusal micellar structure was apparently responsible for the retarded adsorption of this lysolecithin analog to red cells, and the rate of adsorption was probably determined by the rate of escape of single lysophosphatide molecules from the micelles.

1976

15/3,AB/97 (Item 41 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01898660 BIOSIS NO.: 000061058748
NEW DETECTION METHOD OF END POINT IN COLLOID TITRATION USING AN IODIDE ION SELECTIVE ELECTRODE
AUTHOR: ISHIBASHI N; KINA K; TAMURA K
JOURNAL: ANAL LETT 8 (12). 1975 (RECD 1976) 867-872. 1975
FULL JOURNAL NAME: Analytical Letters
CODEN: ANALB
RECORD TYPE: Citation
1975

15/3,AB/98 (Item 42 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01853654 BIOSIS NO.: 000061013720
PHOSPHO LIPASES PART 3 EFFECTS OF IONIC SURFACTANTS ON THE PHOSPHO LIPASE

CATALYZED HYDROLYSIS OF UNSONICATED EGG LECITHIN LIPOSOMES
AUTHOR: GOLDHAMMER A R; JAIN M K; CORDES E H
JOURNAL: J MEMBR BIOL 23 (3-4). 1975 293-304. 1975
FULL JOURNAL NAME: Journal of Membrane Biology
CODEN: JMBBB
RECORD TYPE: Citation
1975

15/3,AB/99 (Item 43 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01709291 BIOSIS NO.: 000060039351
IN-VITRO PHARMACOLOGIC INHIBITION OF RABBIT ADRENAL MICROSOMAL CHOLESTEROL ESTERIFICATION
AUTHOR: MORIN R J; RICHARDS D
JOURNAL: PHARMACOL RES COMMUN 7 (3). 1975 281-288. 1975
FULL JOURNAL NAME: Pharmacological Research Communications
CODEN: PLRCA
RECORD TYPE: Citation
1975

15/3,AB/100 (Item 44 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01656904 BIOSIS NO.: 000059056926
ESTERIFICATION OF CHOLESTEROL BY SUB CELLULAR FRACTIONS FROM SWINE ARTERIES AND INHIBITION BY AMPHIPATHIC AND POLY ANIONIC COMPOUNDS
AUTHOR: MORIN R J; EDRALIN G G; WOO J M
JOURNAL: ATHEROSCLEROSIS 20 (1). 1974 27-39. 1974
FULL JOURNAL NAME: Atherosclerosis
CODEN: ATHSB
RECORD TYPE: Citation
1974

15/3,AB/101 (Item 45 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01635185 BIOSIS NO.: 000059035196
THE INTERACTION OF POLY PEPTIDE COMPONENTS OF HUMAN HIGH DENSITY SERUM LIPO PROTEIN WITH DETERGENTS
AUTHOR: MAKINO S; TANFORD C; REYNOLDS J A
JOURNAL: J BIOL CHEM 249 (23). 1974 7379-7382. 1974
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Citation
1974

15/3,AB/102 (Item 46 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01607337 BIOSIS NO.: 000059007331
IN-VIVO METHOD FOR DETERMINING EFFECTIVENESS OF SPRAY ON BANDAGES CONTAINING ANTI INFECTIVES
AUTHOR: LUONGO M; SCIARRA J J; WARD C O
JOURNAL: J PHARM SCI 63 (9). 1974 1376-1379. 1974
FULL JOURNAL NAME: Journal of Pharmaceutical Sciences

CODEN: JPMSA
RECORD TYPE: Citation
1974

15/3,AB/103 (Item 47 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01603281 BIOSIS NO.: 000059003271
STUDIES ON POLY ADENYLIC-ACID SEQUENCES ASSOCIATED WITH REGENERATING LIVER RNA
AUTHOR: GREENE R F; FAUSTO N
JOURNAL: BIOCHIM BIOPHYS ACTA 366 (1). 1974 23-34. 1974
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Citation
1974

15/3,AB/104 (Item 48 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

00884722 BIOSIS NO.: 000053004854
ETHER CONTAINING LIPIDS OF THE SLIME MOLD PHYSARUM-POLYCEPHALUM PART 2 RATES OF BIOSYNTHESIS
AUTHOR: POULOS A; THOMPSON G A JR
JOURNAL: LIPIDS 6 (7). 1971 470-474. 1971
FULL JOURNAL NAME: Lipids
CODEN: LPDSA
RECORD TYPE: Citation
1971

15/3,AB/105 (Item 49 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

00499125 BIOSIS NO.: 000051089115
THE EFFECT OF POLY PEPTIDE HORMONES ON LIPID MONO LAYERS PART 2 THE EFFECT OF INSULIN ANALOGUES VASOPRESSIN OXYTOCIN THYROCALCITONIN ACTH AND 3 5 CYCLIC AMP ON THE UPTAKE OF CALCIUM IONS BY MONO MOLECULAR FILMS OF MONO OCTA DECYL PHOSPHATE
AUTHOR: KAFKA M S; PAK C Y C
JOURNAL: BIOCHIM BIOPHYS ACTA 193 (1). 1969 117-123. 1969
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Citation
1969

15/3,AB/106 (Item 50 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

00304822 BIOSIS NO.: 000050119822
EFFECTS OF POLY PEPTIDE AND PROTEIN HORMONES ON LIPID MONO LAYERS EFFECT OF INSULIN HORMONE AND PARATHYROID HORMONE ON MONO MOLECULAR FILMS OF MONO OCTA DECYL PHOSPHATE AND STEARIC-ACID
AUTHOR: KAFKA M S; PAK C Y C
JOURNAL: J GEN PHYSIOL 54 (1 PART 1). 1969 134-143. 1969
FULL JOURNAL NAME: Journal of General Physiology
CODEN: JGPLA

RECORD TYPE: Citation
1969

32/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08061933 90198907 PMID: 2317484
Significance and redox state of **SH** groups in pyruvate carrier isolated from bovine heart mitochondria.
Nalecz KA; Muller M; Zambrowicz EB; Wojtczak L; Azzi A
Department of Cellular Biochemistry, Nencki Institute of Experimental Biology, Warsaw, Poland.
Biochimica et biophysica acta (NETHERLANDS) Apr 5 **1990**, 1016 (2) p272-9, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The role and properties of -**SH** groups of purified pyruvate (monocarboxylate) carrier were investigated. After isolation, this protein has all -**SH** groups in the oxidized state. Upon reduction, the carrier can be labelled with eosin-5-maleimide. The shift in apparent Mr after the labelling points to the presence of at least two **cysteine** residues. Pyruvate uptake in the reconstituted system is inhibited by both permeable (eosin-5-maleimide at 1 mM concentration) and impermeable (mersalyl, p-chloromercuribenzoate) -**SH** group reagents. Phenylarsine oxide inhibits pyruvate transport only slightly (20%), but the inhibition is enhanced after preincubation with the substrate.

32/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06612530 89210841 PMID: 2495940
The uncoupling protein dimer can form a disulfide cross-link between the mobile C-terminal **SH** groups.
Klingenberg M; Appel M
Institut fur Physikalische Biochemie, Universitat Munchen, Federal Republic of Germany.
European journal of biochemistry (GERMANY, WEST) Mar 1 **1989**, 180 (1) p123-31, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Isolated uncoupling protein (UCP) can be cross-linked, by various disulfide-forming reagents, to dimers. The best cross-linking is achieved with Cu2+-phenanthroline oxidation. Because cross-linking is independent of UCP concentration and prevented by SDS addition, a disulfide bridge must be formed between the two subunits of the native dimer. Cross-linking is prevented by **SH** reagent and reversed by **SH**-reducing reagents. In mitochondria, cross-linking of UCP with disulfide-forming agents is even more efficient than in isolated state. It proves that UCP is a dimer in mitochondria, before isolation. Disulfide-bridge formation does not inhibit GTP-binding to UCP. Cross-linked UCP re-incorporated in proteoliposomes either before or after cross-linking fully retains the H1-transport function. Rapid cross-linking by membrane impermeant reagents indicates a surface localization of the C-terminus in soluble UCP and projection to the outer surface in mitochondria. Intermolecular disulfide-bridge formation in a dimer requires juxtaposition of identical **cysteines** at the twofold symmetry axis. A rigid juxtaposition of **cysteines** is unlikely, unless intended for a native disulfide bridge. The absence of such a bridge in UCP suggests that juxtaposition of **cysteines** is generated by high mobility. In order to localize the **cysteine** involved, cross-linked UCP was cleaved by BrCN. The CB-7 C-terminal peptide, which contains **cysteines** at positions 287 and 304, disappears. Limited trypsinolytic cleavage, previously shown to occur at Lys-292, removed cross-linking in UCP both in the solubilized and mitochondrially bound state. The cleaved

C-terminal peptide of 11 residues contains only **cystein**-304 which, thus, should be the only one (out of 7 **cysteines** in UCP) involved in the S-S bridge formation. Obviously, the C-terminal location of the **cysteine** , because of its high mobility, permits juxtapositioning for cross-linking. This agrees with predictions from hydrophobicity analysis that the last 14 residues in UCP protrude from the membrane.

Set	Items	Description
S1	3220	CYSTEIN? AND ALKYL?
S2	6	S1 AND (VESIC? OR LIPOSOM?) AND DNA
S3	4	RD (unique items)
S4	1	ALKYLENE (W) SH
S5	203	S1 AND SH
S6	155	RD (unique items)
S7	131	S6 AND PY<1998
S8	11	S7 AND DNA
S9	3011	S1 NOT S2-S8
S10	2360	S9 AND PY<1998
S11	3	S10 AND AMPHIPHIL?
S12	3	RD (unique items)
S13	2357	S10 NOT S11-S12
S14	3	S13 AND LIPOSOM?
S15	2354	S13 NOT S14
S16	381	S15 AND DNA
S17	188	S16 AND CELL?
S18	156	RD (unique items)
S19	19	S18 AND (TRANSFORM? OR TRANSFECT?)
S20	362	S16 NOT S19
S21	3	S20 AND LIPID?
S22	2	RD (unique items)
S23	1	S20 AND CATION?
S24	0	S20 AND SH
S25	44	CYSTEIN? AND DNA AND (ATTRACT?)
S26	36	RD (unique items)
S27	17	S26 AND PY<1998
S28	341	LIPOSOM? AND CYSTEIN?
S29	217	S28 AND PY<1998
S30	157	RD (unique items)
S31	5	S30 AND ALKYL?
S32	10	S30 AND SH